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Synthesis of Star-Shaped Polystyrenes with Glucose in the Chain-End and Core

Harumi Kaga,[1] Shin Yamane,[2] Atsushi Narumi,[1] Toshifumi Satoh,[2,3] Toyoji Kakuchi*[2]*

[1] National Institute of Advanced Industrial Science and Technology (AIST), Sapporo 062-8517, Japan
E-mail: h.kaga@aist.go.jp
[2] Division of Molecular Chemistry, Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan
E-mail: kakuchi@poly-mc.eng.hokudai.ac.jp
[3] Creative Research Initiative "Sousei", Hokkaido University, Sapporo, 060-0808, Japan

Summary: 2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO) was reacted with 4-ethylphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside using *tert*-butyl hydroperoxide and cobalt(II)acetate tetrahydrate in acetonitrile. The reaction provided 4-[1'-(2",2",6",6"-tetramethyl-1"-piperidinyloxy)-ethyl]phenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside, glycoconjugated initiator. Star-shaped polystyrene architectures in which glucose was covalently bonded in the core and chain-end were successfully prepared from the glycoconjugated initiator, styrene, and 1,4-divinylbenzene as starting materials.

Keywords: amphiphiles; living polymerization; microgels; radical polymerization; star polymers

Introduction

Three-dimensional polymeric architectures with functional groups in their interior or periphery have attracted much attention, because they have the potential to generate novel technological applications.[1-4] For example, Bosman et al. reported a modular approach for the synthesis of star polymers with functional groups to permit application as multifunctional hosts for hydrogen bonding and scaffolds for catalytic groups.[1] Saccharides are known to show a strong hydrophilic property derived from their multiple hydroxyl groups and possess biological functions based on specific molecular and cell recognition ability; hence, they are attractive molecules for conjugated polymeric architectures. There have been few reports, however, on introducing saccharides into star polymers. For examples, we reported that a star polymer with a glycoconjugated core was prepared using vinyl saccharide.[5] Ohno et al.,[6] Stenzel-Rosenbaum and Davis[7] and our group[8] reported the living radical polymerization with a cyclodextrin-based multifunctional initiator producing star-shaped polymers.

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We report here that 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) reacts with 4-ethylphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside to provide 4-[1'-(2",2",6",6"-tetramethyl-1"-piperidinyloxy)-ethyl]phenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside, the glycoconjugated initiator **1** (Scheme 1). Star-shaped polystyrene architectures in which glucose was covalently bonded in their core and chain-ends were prepared from the glycoconjugated initiator, styrene, and 1,4-divinylbenzene as starting materials, as illustrated in Scheme 2.

Experimental Part

Materials. Styrene (St) (Kanto Chemical Co., >99.0 %), 1,4-divinylbenzene (DVB) (Aldrich, tech., a mixture of isomers, 80%), and *m*-xylene (Kanto Chemical Co., >99.0 %) were distilled just before use. Acetonitrile (Junsei Chemical Co. Japan, >99.5 %) was distilled over CaH_2 prior to use.

Measurements. Size exclusion chromatography (SEC) was performed at 40°C in chloroform (1.0 $mL\cdot min^{-1}$) using a Jasco GPC-900 system equipped with a Shodex KF-804L column (linear, 8 mm × 300 mm) and a Shodex KF-805L column (linear, 8 mm × 300 mm). The preparative SEC was performed at 23°C in chloroform (3.8 $mL\cdot min^{-1}$) using a JAI LC-908 equipped with two JAI JAIGEL-3H polystyrene columns (20 mm × 600 mm) and JAI UV-310 and JAI RI-5HC detectors. The static laser light scattering (SLS) measurement was performed in toluene at 25 °C on an Otsuka Electronics DLS-7000 light scattering spectrophotometer ($\lambda = 632.8$ nm; four-point measurements; $c = 2 \sim 10$ mg/mL). The refractive index increment (*dn*/*dc*) was measured in toluene at 25 °C on an Otsuka Electronics DRM-1021 double beam-differential refractometer ($\lambda = 632.8$ nm).

Glycoconjugated Initiator, 1. The procedure was similar to that previously reported.[9] To a mixture of 4-ethylphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside [10] (2.01 g, 4.44 mmol), TEMPO (902 mg, 5.77 mmol), cobalt(II)acetate tetrahydrate (110 mg, 0.44 mmol), and powdered molecular sieves 4A in acetonitrile (5 mL) was added *tert*-butyl hydroperoxide (1.50 g, 13.3 mmol) under an argon atmosphere. The color of the reaction solution changed from dark orange to dark green. After stirring for 14 h at room temperature, the reaction mixture was filtered off and the solvent in the filtrate was evaporated. The residue was diluted with dichloromethane and then washed with H_2O. After the organic layer was dried with anhydrous sodium sulfate and evaporated to dryness, the crude product was purified by chromatography on silica gel with hexane/acetone (4/1, v/v) to give **1** as a white solid. Yield:

680 mg (25.2 %). ^{1}H NMR (400 MHz, CDCl3): δ (ppm) = 7.24 (d, J = 8.5 Hz, 2H, Ar), 6.93 (d, J = 8.5 Hz, 2H, Ar), 5.32-5.07 (m, 4H, H-1, 2, 3, 4), 4.75 (q, J = 6.6 Hz, 1H, -CH-), 4.31 (dd, J = 5.5 Hz, J = 12.3 Hz, 1H, H-6), 4.17 (dd, J = 2.32 Hz, J = 12.3 Hz, 1H, H-6), 3.90-3.85 (m, 1H, H-5), 2.08, 2.06, 2.05, 2.04 (each s, 12H, CH_3), 1.48-1.40 (br, 6H, CH_2), 1.44 (d, J = 6.6 Hz, 3H, CH_3), 1.28, 1.15, 1.01, 0.66 (each br s, 12H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 170.5, 170.1, 169.3, 169.2, 155.6, 140.8, 127.6, 116.4, 99.1, 82.2, 72.7, 71.8, 71.1, 68.3, 61.9, 59.6, 40.2, 34.3, 23.4, 20.6, 20.5, 20.2, 17.1. IR (NaCl, cm^{-1}): 1755, 1368. $[\alpha]_D^{23}$ = –10.6° (*c* 5.0, $CHCl_3$). $[\alpha]_{365}^{23}$ = –37.8° (*c* 5.0, $CHCl_3$). Anal. Calcd. for $C_{31}H_{45}NO_{11}$: C, 61.27; H, 7.46; N, 2.30 Found: C, 61.13; H, 7.49; N, 2.08.

Polystyrene End-functionalized with Acetyl Glucose, 2. A mixture of styrene (25.0 g, 240 mmol) and **1** (584 mg, 0.961 mmol) in a 50-mL round-bottom flask with a septum was degassed by three freeze/thaw cycles, sealed under argon, and heated at 120 °C for 6 h. After cooling in liquid nitrogen, the mixture was diluted with chloroform (30 mL) and then precipitated in methanol (ca. 2 L). The precipitate was purified by reprecipitation with chloroform-methanol and dried *in vacuo* to give **2** as a white powder. Yield: 10.2 g (40.9 %). $M_{w,\,SEC}$ = 10.3 kg·mol^{-1}, M_w/M_n = 1.10. $[\alpha]_{365}^{23}$ = –2.1° (*c* 5.0, $CHCl_3$).

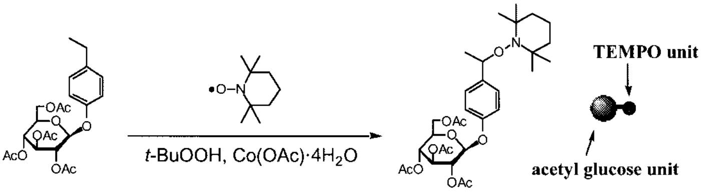
Star-shaped Polystyrene with Acetyl Glucose. The general procedure is as follows. A mixture of PS-TEMPO (1.00 g, 0.10 mmol), **1** (60.8 mg, 0.10 mmol), DVB (639 mg, ca. 3.93 mmol), and *m*-xylene (4.8 mL) was degassed by three freeze/thaw cycles, sealed under argon, and heated at 138 °C for 20 h. After cooling in liquid nitrogen, the mixture was diluted with chloroform (16 mL), and then poured into methanol (ca. 1 L). The precipitate was purified by reprecipitation with chloroform-methanol and dried *in vacuo* to give a white powder. Yield: 1.48 g (94.2 % based on the total feed of PS-TEMPO, **1** and DVB). $M_{n,SEC}$ = 81.6 kg·mol^{-1}, M_w/M_n = 2.23. The product (1.48 g) was redissolved in chloroform (16 mL). The solution (2 mL) was subjected to preparative SEC and the eluents with retention times of 36-49 min and 49-61 min were fractionalized. This procedure was repeated eight times. The combined eluents with the retention times of 36-49 min were evaporated and poured into methanol. The precipitate was filtered and dried *in vacuo* to give **2** as a white powder (1.11 g, 74.9 %). $M_{w,SEC}$ = 118 kg·mol^{-1}, M_w/M_n = 1.51. $M_{w,SLS}$ = 367 kg·mol^{-1}, $[\alpha]_{365}^{23}$ = –2.3° (*c* 5.0, $CHCl_3$). The combined eluents with the retention times of 49-61 min were evaporated, precipitated in methanol, filtered, and dried *in vacuo* to give unreacted PS-TEMPO (372 mg, 25.1 %).

Star-shaped Polystyrene with Glucose. The general procedure is as follows. A solution of

2 ($M_{w,SLS}$ = 367 kg·mol^{-1}, 300 mg) in dry THF (2 mL) was added to a dry THF solution containing 2 wt-% sodium methoxide (2 mL). The reaction mixture was stirred for 24 h at room temperature, precipitated in methanol (250 mL), filtered, and washed with water and methanol. The precipitate was finally purified by reprecipitation with chloroform-methanol and dried *in vacuo* to give **5** as a white powder (279 mg, 93.3 %). $M_{w,SLS}$ = 363 kg·mol^{-1}.

Results and Discussion

Star-shaped Polystyrene with Acetyl Glucose in the Core. 2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO) was reacted with 4-ethylphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside using *tert*-butyl hydroperoxide (*t*-BuOOH) and cobalt(II)acetate tetrahydrate (Co(OAc)·4H_2O) in acetonitrile at room temperature under argon as shown in Scheme 1. The reaction afforded 4-[1'-(2",2",6",6"-tetramethyl-1"-piperidinyloxy)-ethyl]phenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside, glycoconjugated initiator **1**. The advantage of the procedure is that it is easy and safe to operate.[9]



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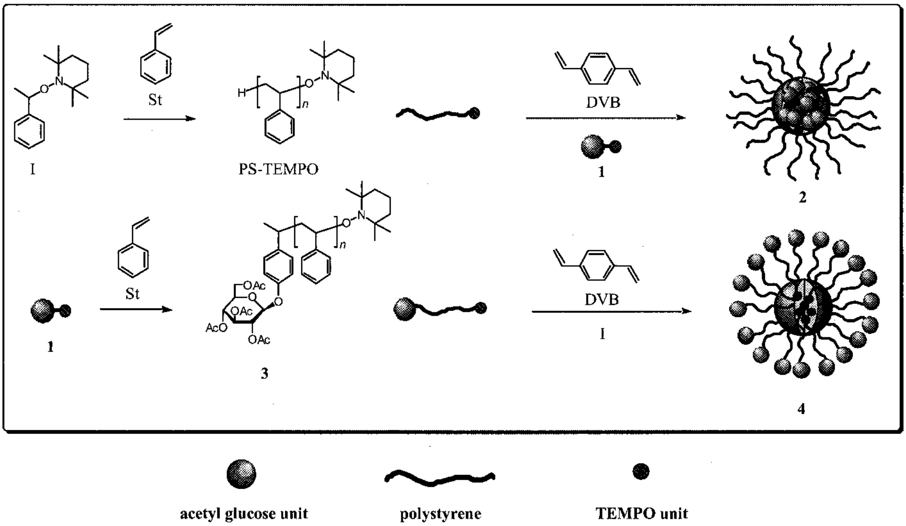
Scheme 1. Synthesis of glycoconjugated initiator **1**.

Star-shaped polystyrene with acetyl glucose in the core was prepared from **1**, styrene (St), and 1,4-divinylbenzene (DVB) as starting materials (Scheme 2). In the first step, St was polymerized with 1-phenyl-1-(2',2',6',6'-tetramethyl-1'-piperidinyloxy)ethane[11] (I) using the molar ratio of St and I ([St]/[I]) of 250 at 120 °C for 6 h. The polymerization produced TEMPO-terminated polystyrene (PS-TEMPO) with a weight-average molecular weight ($M_{w,SEC}$) of 10.0 kg·mol^{-1} and a polydispersity (M_w/M_n) of 1.09, which were based on linear polystyrene standards using a differential refractometer (RI) detector.[5]

In the second step, the coupling reaction of PS-TEMPO was performed using DVB as a linking agent and **1** as an additive in *m*-xylene at 138°C for 20 h (Scheme 2). The molar ratio of PS-TEMPO and **1** ([PS-TEMPO]/[**1**]) was a constant value of 1/1, while the ratio of DVB and total TEMPO units ([DVB]/[PS-TEMPO] + [**1**], F_{DVB}) was changed to optimize the coupling reaction (Table 1). The reaction with the F_{DVB} of 14, 17, 20, and 22 afforded the original products in 89.8, 94.4, 94.8, and 96.9 % yields, respectively, which completely passed though a 0.45 μm PTFE membrane filter.



Scheme 2. Synthesis of star-shaped polystyrenes with acetyl glucose in the core and chain-end (**2** and **4**, respectively).

Table 1. Synthesis and characterization of star-shaped polystyrene with acetyl glucose

Feed			Star polymer [a]						
Arm-polymer	Additive	F_{DVB}	Sample	W_{star} [b]	$M_{w,SLS}$ [c] kg·mol^{-1}	d [d] nm	$[\alpha]_{365}$ [e] deg	N_{arm} [f]	N_1 [g]
PS-TEMPO	**1**	14	**2**	0.612	93.6	12	–2.1	6	9
PS-TEMPO	**1**	17	**2**	0.704	211	17	–2.2	12	20
PS-TEMPO	**1**	20	**2**	0.749	367	20	–2.3	21	37
PS-TEMPO	**1**	22	**2**	0.838	1160	40	–2.1	64	104
3	I	20	**4**	0.750	385	18	–1.4	23	23

[a] Prepared by fractionation of the original product, which was obtained from the coupling reaction.
[b] The weight fraction of star-shaped polymer in the original product.
[c] Determined by SLS measurement.
[d] Determined by DLS measurement.
[e] Measured in $CHCl_3$ at 23 °C (*c* 5.0).
[f] The arm-number.
[g] The number of the **1** unit.

Figure 1b ~ e shows the SEC traces of the original products, indicating that a high molecular weight polymer with an $M_{w,SEC}$ above 10 kg·mol^{-1} formed, while unreacted PS-TEMPO remained. The unreacted PS-TEMPO was separated using preparative SEC from the original products to give a high molecular-weight polymer **2**. Table 1 summarizes the characterization of **2**.

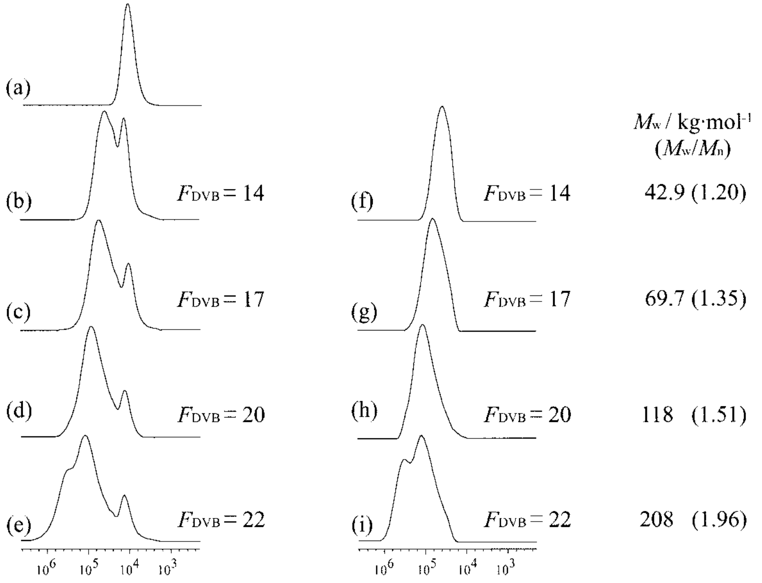


Figure 1. SEC traces of (a) PS-TEMPO, (b)~(e) the original products obtained from the coupling reactions of PS-TEMPO using DVB as a linking agent and **1** as an additive, and (f)~(i) **2**.

Figures 1f ~ i show the SEC traces of **2** with $M_{w,SEC}$'s of 42.9 ~ 208 kg·mol^{-1} and M_w/M_n's of 1.20 ~ 1.96. The $M_{w,SEC}$'s of **2** were 4 ~ 20 times that of PS-TEMPO. However, $M_{w,SEC}$ was the apparent molecular weight on the basis of linear polystyrene standards. Hence, **2** was characterized using a static laser light scattering (SLS) measurement to determine the absolute weight-average molecular weight, $M_{w,SLS}$. The $M_{w,SLS}$ values of 93.6 ~ 1160 kg·mol^{-1} (Table 1) were found to be greater than the respective $M_{w,SEC}$ values, suggesting that the hydrodynamic volume of **2** was considerably smaller compared to the linear polystyrene with the same molecular weight. It was found that **2** existed as particles in toluene with average diameters (*d*) of 12 ~ 40 nm, which were determined by dynamic laser light scattering (DLS) measurement. Thus, **2** was assignable to a star-shaped architecture.

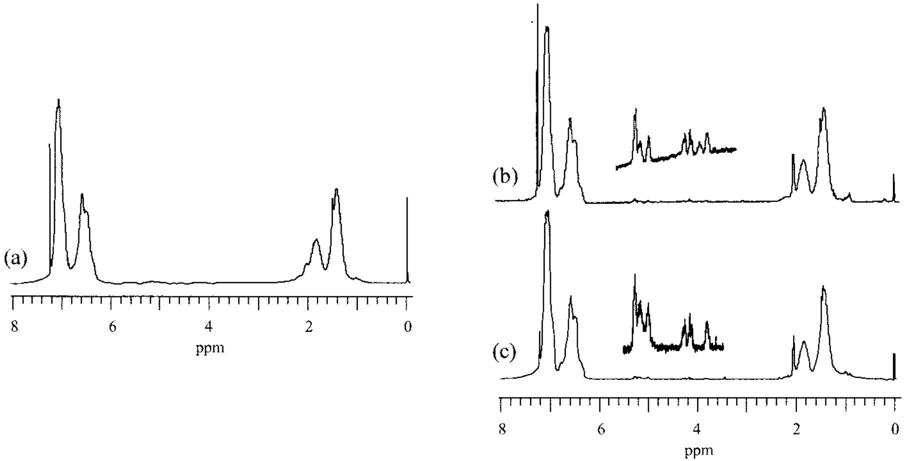


Figure 2. ^{1}H-NMR spectra of (a) **2**, (b) **3**, and (c) **4** in $CDCl_3$.

The introduction of the **1** unit had to be confirmed; however, the signal due to the **1** unit did not appear in the ^{1}H-NMR spectra for **2** (Figure 2a). However, **2** showed an $[\alpha]_{365}^{23}$ (c 5.0 $CHCl_3$) ranging form –2.1° ~ –2.3°. In addition, adsorption due to the acetyl group appeared at 1760 cm^{-1} in the IR spectra of **2**. These results suggested that the signals in the ^{1}H-NMR spectra should be extremely broadened to the point of disappearing, because the **1** unit was bonded to the core of **2**, so that intramolecular mobility of the protons was significantly eliminated. Thus, **2** was assigned to star-shaped polystyrenes with acetyl glucose in the core. The weight fractions of **2** in the original product (W_{star}'s) ranged from 0.612 ~ 0.838, which were determined from the isolated yields. The number of the arm and the **1** unit (N_{arm} and N_1) were 6 ~ 64 and 9 ~ 104 for **2**, respectively, which were calculated from the yields and the $[\alpha]_{365}^{23}$ values. The d, N_{arm}, and N_1 were found to increase with the increasing F_{DVB}. However, an undesirable shoulder due to a highly coupled product appeared for the product with an F_{DVB} of 22 (Figure 1e). Furthermore, the reaction with an F_{DVB} value higher than 22 produced a much more highly crosslinked species. Reversibly, a large amount of PS-TEMPO remained after the reaction with an F_{DVB} of 14 (Figure 1b). Hence, the F_{DVB} of 17 ~ 20 was found to be the optimized condition for the system.

Star-shaped Polystyrene with Acetyl Glucose in the Chain-end. In the first step, St was polymerized with **1** at 120 °C (bulk, [St]/[**1**] = 250) for 6 h to afford **3** in a 41 % yield (Scheme 2). Figure 3a shows the SEC trace of **3** with an $M_{\text{w,SEC}}$ of 10.3 kg·mol^{-1} and an

M_w/M_n of 1.10. Figure 2b shows the ^{1}H-NMR spectrum of **3**, in which the signals due to polystyrene appeared at 1.2 ~ 2.0 ppm and 6.2 ~ 7.4 ppm along with the characteristic signals due to the **1** unit at 0.2 ~ 1.2 ppm (the methyl protons in the TEMPO moiety) and 3.4 ~ 5.4 ppm (the methine and methylene protons in the saccharide moiety). Hence, **3** was assigned to a polystyrene end-functionalized with acetyl glucose. The characterization by a thin layer chromatograph equipped with a flame ionization detector (TLC-FID) indicated that the introduction of acetyl glucose into the initiating chain-end was found to occur in a quantitative fashion for **3**, as reported elsewhere.[12] The specific rotation ($[\alpha]_{365}^{23}$, *c* 5.0 $CHCl_3$) of **3** was –2.1°, whose sign was consistent with that of **1** ($[\alpha]_{365}^{23} = -37.8°$).

In the second step, the coupling reaction of **3** with DVB was performed under the optimized conditions for the preparation of **2**, i.e., at 138 °C for 20 h using a molar ratio of **3** and I ([**3**]/[I]) of 1/1 and a ratio of DVB and total TEMPO unit ([DVB]/[**3**] + [I], F_{DVB}) of 20 (Table 1). The reaction afforded an original product in 94.8 % yield, which completely passed though the 0.45 μm PTFE membrane filter. A small amount of unreacted **3** was removed from the product using preparative SEC to obtain **4** with an $M_{w,SEC}$ of 97.2 kg·mol^{-1} and an M_w/M_n of 1.37 (Figure 3c). Table 1 lists the characterization of **4**. The DLS measurements indicated **4** stably suspended as particles with a *d* of 18 nm in toluene. The $M_{w,SLS}$ of 385 kg·mol^{-1} was larger than the $M_{w,SEC}$. Figure 2c shows the ^{1}H-NMR spectrum of **4**. The signals of **4** were very similar to those of **3**. In addition, **4** showed the $[\alpha]_{365}^{23}$ (*c* 5.0, $CHCl_3$) of –1.4°, which was slightly a smaller value than that of **3**. These results indicated that **4** was assignable to star-shaped polystyrene with acetylated glucose in the chain-end.

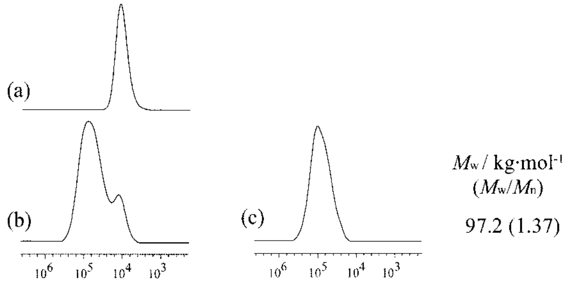
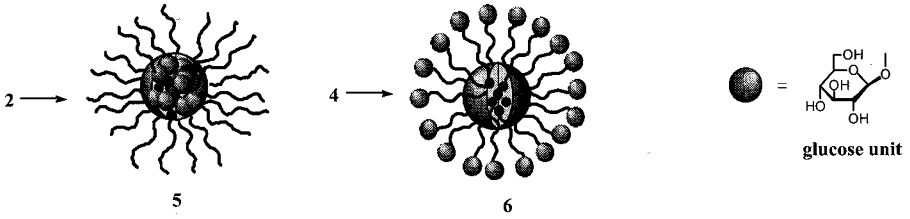


Figure 3. SEC traces of (a) **3**, (b) the original product obtained from the coupling reaction of **3** using DVB as a linking agent, and (c) **4**.

As expected, the N_{arm} of 23 for **4** was a value similar to that (21) for **2** (F_{DVB} = 20) as listed in Table 1. However, the N_I of 23 for **4** was smaller than that (37) for **2** (F_{DVB} = 20). These results suggest that the reactivity of **1** and I is higher than that of PS-TEMPO and **3**, respectively, for the coupling reactions.

Star-shaped Polystyrene with Glucose in the Chain-End and Core. Deacetylation of **2** and **4** was achieved using sodium methoxide in dry THF to afford star-shaped polystyrenes with glucose in the core and chain-end, **5** and **6** (Scheme 3). The polymers **5** and **6** are constituted of a three-dimensional structure in a nanoscale size, in which glucose is located at the periphery or interior. Hence, **5** and **6** have potential to possess the ability, for example, to entrap a polar molecule at their hydrophilic periphery or interior.

We mention here the solution properties of **5** and **6**. It was reported that linear polystyrene with saccharide in the chain-end formed a reversed-type polymeric micelle in the good solvents for polystyrene.[12,13] Hence, we cannot exclude the possibility that **5** and **6** exist as star-star aggregates in the good solvents for polystyrene, in which the driving force is attributable to the intermolecular aggregation of multiple hydroxyl groups in the saccharide. However, the $M_{\mathrm{w,SLS}}$ values of **5** and **6** were very similar to those of **2** and **4**, respectively. As one example, the $M_{\mathrm{w,SLS}}$ of **5** was 363 kg·mol^{-1} in $CHCl_3$, which was obtained through deacetylation of **2** ($M_{\mathrm{w,SLS}}$ = 367 kg·mol^{-1}). Hence, **5** and **6** were found to exist in $CHCl_3$ as unimers.



Scheme 3. Synthesis of star-shaped polystyrene with glucose.

Conclusion

Glycoconjugated initiator for the TEMPO-mediated living radical polymerization, **1**, was prepared and found to be a useful tool for constructing star-shaped polystyrene architectures with saccharide in the interior and periphery.

[1] A. W. Bosman, R. Vestberg, A. Heumann, J. M. J. Fréchet, C. J. Hawker, *J. Am. Chem. Soc.* **2003**, *125*, 715.
[2] D. A. Tomalia, J. M. J. Fréchet, *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 2719.
[3] S. E. Stiriba, H. Frey, R. Haag, *Angew. Chem., Int. Ed.* **2002**, *41*, 1329.
[4] K. L. Wooley, *J. Polym. Sci., Polym. Chem.* **2000**, *38*, 1397.
[5] A. Narumi, T. Satoh, H. Kaga, T. Kakuchi, *Macromolecules* **2002**, *35*, 699.
[6] K. Ohno, B. Wong, D. M. Haddleton, *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 2206.
[7] M. H. Stenzel-Rosenbaum, T. P. Davis, *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 4498.
[8] T. Kakuchi, A. Narumi, T. Matsuda, Y. Miura, N. Sugimoto, T. Satoh, H. Kaga. *Macromolecules* **2003**, *36*, 3914.
[9] N. Sugimoto, A. Narumi, T. Satoh, H. Kaga, T. Kakuchi, *Polym. Bull.* **2003**, *49*, 337.
[10] M. Stephane, B. Claude, L. Jean-Pierre, *Tetrahedron Lett.* **1993**, *34*, 4531.
[11] C. J. Hawker, G. G. Barclay, A. Orellana, J. Dao, W. Devonport, *Macromolecules* **1996**, *29*, 5245.
[12] T. Kakuchi, A. Narumi, T. Matsuda, Y. Miura, N. Sugimoto, T. Satoh, H. Kaga, *Macromolecules* **2003**, *36*, 3909.
[13] S. Loykulnant, A. Hirao, *Macromolecules* **2001**, *101*, 2921.