Synthesis of Star-Shaped Polystyrenes with Glucose- and Maltohexaose-Conjugated Core through Nitroxide-Controlled Free-Radical Polymerization

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Summary: Coupling reactions of TEMPO-terminated polystyrene (PS-TEMPO) with divinylbenzene were performed in the presence of vinyl saccharides **1**, successfully producing star-shaped polystyrenes with glycoconjugated core **2**. Amphiphilic star-shaped polystyrenes with cores containing saccharide as hydrophilic segments **3** were obtained by the deacetylation of **2**, which exhibited an encapsulation ability toward methyl orange (MO) in chloroform. A positive Cotton effect was observed in the CD spectrum for the MO/**3** in the adsorption area of MO, indicating that MO existed in a chiral segment, i.e., the glycoconjugated core.

Introduction

Recently nitroxide-controlled free-radical polymerization have been interestingly developed for the syntheses of a variety of macromolecular architectures.[1,2] Star-shaped polystyrenes, as an example, were formed via "arm first" method, i.e., the coupling reaction of preformed alkoxyamine-terminated polystyrenes using a difunctional crosslinking reagent.[3-8] This free-radical process can be applicable to a wide variety of functional groups, and it is of great interest to extend this process to the synthesis of functionalized star-shaped polymers.

We now report the synthesis of star-shaped polystyrenes with glucose- and maltohexaose-conjugated core (**3a**-**b**) through three steps, i.e., (i) preparation of 2,2,6,6-tetramethylpiperidinyloxy-terminated polystyrene (PS-TEMPO), (ii) coupling

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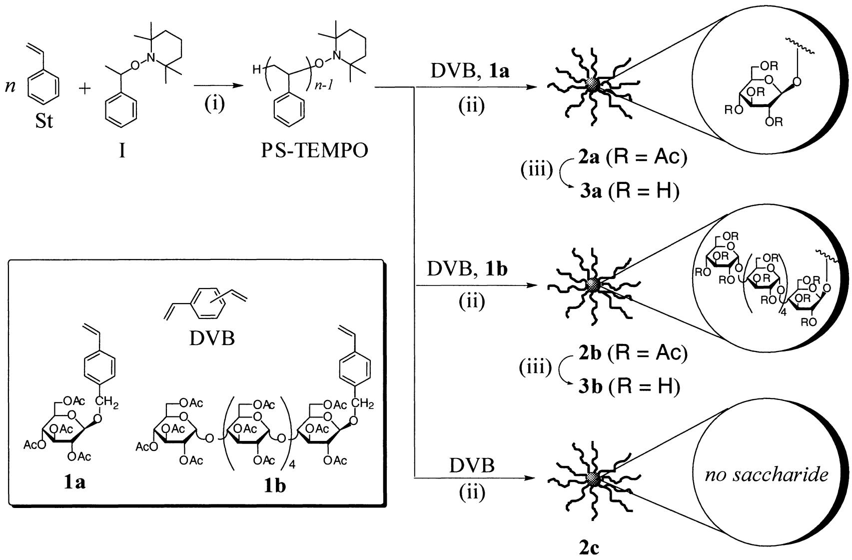
reactions of PS-TEMPO using divinylbenzene (DVB) as a linking agent in the presence of glucosyl and maltohexaosyl styrene peracetates (**1a**-**b**), and (iii) deacetylation of **2a**-**b**, as described in Scheme 1. Because polymer **3** possesses multiple hydroxyl groups in the core, it is expected to have interesting hydrophilic properties. Thus, we report the encapsulation ability of **3** toward water-soluble molecules such as methyl orange.



Scheme 1. Synthetic procedure: (i) bulk, 120 °C, 6 h, [St]/[I] = 200/1. (ii) solvent; *m*-xylene, 138 °C, 20 h, [PS-TEMPO]/[DVB]/[**1**] = 1/31/4, PS-TEMPO/*m*-xylene = 1.0/4.5, g/mL. (iii) NaOMe-MeOH, THF, room temperature, overnight.

Results and Discussion

Synthesis of Arm Polymer. Styrene (St) was polymerized using 1-phenyl-1-(2',2',6',6'-tetramethyl-1'-piperidinyloxy)-ethane[9] as an initiator (I) to afford PS-TEMPO with a weight-average molecular weight ($M_{w,SEC}$) of 1.0 × 10^4 g/mol and a polydispersity (M_w/M_n) of 1.09, which were estimated from the linear polystyrene-calibrated size exclusion chromatography (SEC) using a differential refractometer (RI) detector. The weight-average molecular weight ($M_{\mathrm{w,SLS}}$) of 1.1 × 10^4 g/mol, which was determined by a static laser light scattering (SLS) measurement, was similar to the $M_{\mathrm{w,SEC}}$ value.

Synthesis and Characterization of Star-shaped Polymer 2. Coupling reactions of PS-TEMPO using 1,4-divinylbenzene (DVB) (Aldrich, tech., mixture of isomers, 80%) were carried out in the presence of 4-vinylbenzyl glucoside peracetate (**1a**)[10] or 4-vinylbenzyl maltohexaoside peracetate (**1b**)[10]. The obtained products were soluble in good solvents for polystyrene, such as toluene, $CHCl_3$ and dioxane. The SEC chromatograms of the products exhibited two peaks. A small amounts of low-molecular weight polymers ($M_{\mathrm{w,SEC}}$= ca. 1.0 × 10^4 g/mol) was removed from the products using preparative SEC giving high molecular weight polymers **2a** ($M_{\mathrm{w,SEC}}$ = 7.5 × 10^4 g/mol, $M_{\mathrm{w}}/M_{\mathrm{n}}$= 1.36) and **2b** ($M_{\mathrm{w,SEC}}$ = 7.2 × 10^4 g/mol, $M_{\mathrm{w}}/M_{\mathrm{n}}$ = 1.35). In the absence of **1**, the same coupling reaction was also performed, followed by separation using preparative SEC to produce **2c** ($M_{\mathrm{w,SEC}}$ = 8.3 × 10^4 g/mol, $M_{\mathrm{w}}/M_{\mathrm{n}}$= 1.36). The yields of **2a-c** from the unpurified products were 82-83 %, while the yields of **2** (weight, g) from the total feed of the starting materials (weight, g) were 69 % for **2a**, 59 % for **2b**, and 72 % for **2c**.

Table 1 shows the weight-average molecular weights ($M_{\mathrm{w,SLS}}$) of **2**, which were determined by SLS measurements. The $M_{\mathrm{w,SLS}}$ values were 2.9 × 10^5 for **2a**, 2.3 × 10^5 for **2b**, and 3.2 × 10^5 g/mol for **2c**. These values were 3 ~ 4 times greater than the $M_{\mathrm{w,SEC}}$ values, indicating that the hydrodynamic volumes of **2** were considerably small compared to the linear polystyrene with the same molecular weight, i.e., a star-shaped polymer should be produced in the coupling reactions even in the presence of **1**.

The $[\alpha]_D^{23}$ (*c* 1.0, $CHCl_3$) values were −3.5° for **2a** and +15.8° for **2b**, whose signs were consistent with that of homopolymer derived from **1a** and **1b**, respectively. This result indicated that the **1** units are introduced into the DVB microgel core in a star-shaped polymer. The introduction of the **1a-b** units in **2a-b** was also confirmed by the ^{1}H-NMR spectra.

The weight fractions of St, **1**, and DVB units in **2** (W_{St}, W_1, and W_{DVB}, respectively) were calculated in order to determine the arm-numbers (N_{arm}) and the core-composition ratios ([**1** unit]/[DVB unit]) of **2**. Throughout the purification procedure of **2**, the St unit is completely recovered (little if any loss by the absorbent). Hence, there is the following relation according to the stoichiometric balance of the St unit, giving the W_{St} values of **2**.[11]

$$\text{Feed of PS-TEMPO} = (W_{St} \times \text{Yield of } \mathbf{2}) + (\text{Yield of unreacted PS-TEMPO}) \quad (1)$$

The W_1 values equal the $[\alpha]_D^{23}$ of **2a** and **2b** divided by that of poly-**1a** ($[\alpha]_D^{23} = -50.4$) and poly-**1b** ($[\alpha]_D^{23} = +112.9$). The following relation gave the W_{DVB} values of **2**.

$$W_{St} + W_1 + W_{DVB} = 1 \quad (2)$$

The N_{arm} and the [**1** unit]/[DVB unit] values were was determined by the following equations 3 and 4, respectively, and shown in Table 1.

$$N_{arm} = (W_{St} \times M_{w,SLS} \text{ of } \mathbf{2}) \,/\, (M_{w,SLS} \text{ of PS-TEMPO}) \quad (3)^{[12]}$$

$$[\mathbf{1}\text{ unit}]/[\text{DVB unit}] = (W_1 / \text{M.W. of } \mathbf{1}) \,/\, (W_{DVB} / \text{M.W. of DVB}) \quad (4)$$

Table 1. Characterization of star-shaped polymer.

Sample	$M_{w,SLS}$ g/mol	Weight fractions			Arm-number	Core-composition
		W_{St}	W_1	W_{DVB}	N_{arm}	[**1** unit]/[DVB unit]
2a	2.9×10^5	0.70	0.07	0.23	18	0.09
2b	2.3×10^5	0.62	0.15	0.23	13	0.04
2c	3.2×10^5	0.73	-	0.27	21	-

Synthesis and Amphiphilic Property of Star-shaped Polymer 3. The deacetylation of **2a** and **2b** was carried out by alkaline hydrolysis using sodium methoxide in dry THF to afford star-shaped polystyrenes having a glucose- and maltohexaose-conjugated core (**3a** and **3b**, respectively). The solubility of **3a** was similar to that of **2a**, i.e., soluble in toluene, $CHCl_3$, and dioxane. On the other hand, the solubility of **3b** was different from that of **2b**, i.e., **3b** was insoluble in toluene. This result should be attributable to the strong hydrophilic property of maltohexaose.

The star-shaped polymers **3** constitute a novel structure, i.e., saccharide molecules protected by many polystyrene arms, therefore, they are expected to show a characteristic amphiphilic property. To encapsulate a water-soluble molecule in good solvents for polystyrene is one of the desired abilities of **3**. To the respective solutions of **3** in $CHCl_3$ was added methyl orange (MO), the heterogeneous mixtures (**3**/MO/$CHCl_3$ = 20/20/1, g/g/L) were shaken for 18 h at 40 °C, and then undissolved MO were removed using membrane filters. The characteristic absorption due to MO appeared in the visible area from 350 to 550 nm for the UV-vis spectra of the filterates (MO/**3**). The absorbance of MO/**3b** (abs. = 1.04 at λ = 432 nm) was considerably larger than that of MO/**3a** (abs. = 0.22 at λ = 428 nm). This fact indicates that encapsulation remarkably increased with the increasing hydrophilic property of the core in **3**.

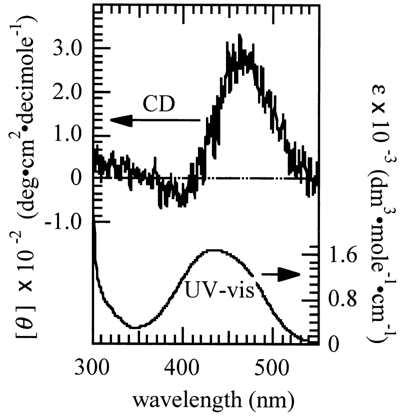


Figure 1. CD (upper line) and UV-vis (bottom line) spectra of MO/**3b** system, recorded in chloroform using a path length of 1 mm.

The chiroptical property of MO/**3b** was examined using CD spectroscopy (Figure 1). In the CD spectrum, the positive Cotton effect was observed in the area from 400 to 550 nm corresponding to the absorption of MO, indicating that MO existed in a chiral segment, i.e., the glycoconjugated core in **3**.

Conclusion

Coupling reactions of PS-TEMPO using DVB as a linking agent were performed in the presence of vinyl saccharides (**1**), followed by deacetylation to give glycoconjugated star-shaped polystyrenes with a core (**3**). Star-shaped polymers **3** exhibited encapsulation ability toward methyl orange in chloroform. A positive Cotton effect was observed in the CD spectrum for the MO/**3** system, indicating that MO existed in a chiral segment, i.e., the glycoconjugated core in **3**.

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