Precision Synthesis of (1→6)-α-D-Glucopyranan by Cationic Ring-Opening Polymerization of 1,6-Anhydro-2,3,4-Tri-*O*-Allyl-β-D-Glucopyranose

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Summary: The ring-opening polymerization of 1,6-anhydro-2,3,4-tri-*O*-allyl-β-D-glucopyranose (**2**) has been carried out using various cationic initiators. For the condition of [**2**]/[BF_3•OEt_2] = 20 at -15 °C for 90 h, the polymer yield, M_w and M_w/M_n of the polymer obtained were 79 %, 215,600 and 3.45, respectively. In order to study the living characteristic of the polymerization of **2**, the cationic ring-opening bulk polymerization initiated by trimethylsilyl trifluoromethanesulfonate (TMSOTf) was carried out under the condition of [**2**]/[TMSOTf] = 1000 at -15 °C. The M_w value increased in proportion to conversion until c.a. 30 % and below. The M_w/M_ns of resulting polymers were very narrow, e.g., the M_w/M_n value was 1.2 and below, which was smaller than that for the solution polymerization using BF_3•OEt_2. These results indicated that the ring-opening bulk polymerization of **2** using TMSOTf was living-like.

Introduction

In carbohydrate chemistry, protection of the hydroxyl group is important for the synthesis of desired mono- and oligosaccharides, so that there are many protective groups, such as amides, esters, and ethers. For the synthesis of carbohydrate polymer, various types of mono- and oligosaccharide monomers were designed using suitable protective groups, such as the benzyl ether and the ortho ester. In particular, the ring-opening polymerization of anhydro sugar protected with the benzyl ether is the most established method, e.g., Schuerch et al. reported the cationic ring-opening polymerization of 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-glucopyranose leading to highly stereoregulated polymers.[1-4] However, cleavage of the benzyl ether linkage in the polymer, which was performed using Na/liq. NH_3, is not suitable for a preparative method.

Recently, we reported that the facile method of synthesizing (1→6)-α-D-glucopyranan,

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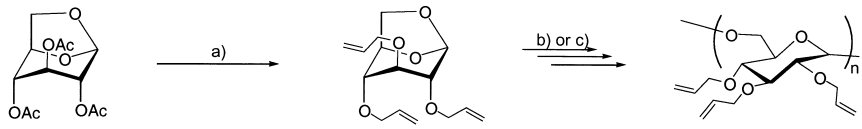
as shown in Scheme 1, and indeed, the allyl ether used as a protecting group was easily removed from 2,3,4-tri-*O*-allyl-(1→6)-α-D-glucopyranan (**3**).[5,6] Thus, it is interesting to expand the scope of the allyl ether-protecting method, for instance, the precision control of molecular weight, polydispersity, and chain ends of synthetic polysaccharides should be promised well-defined (1→6)-α-D-glucopyranan such as a polysaccharide macromonomer. Herein, we report the ring-opening polymerization of 1,6-anhydro-2,3,4-tri-*O*-allyl-β-D-glucopyranose (**2**) using alkyl and silyl trifluoromethanesulfonates as new types of cationic initiators. In particular, trimethylsilyl trifluoromethanesulfonate (TMSOTf) was an effective initiator for the bulk polymerization of **2** leading to relatively narrow polydispersed 2,3,4-tri-*O*-allyl-(1→6)-α-D-glucopyranan (**3**).



1 **2** **3**

a) CH_2=CH-CH_2-Br,n-Bu_4NHSO_4, powder NaOH/$CH_3C_6H_5$
b) solution polymerization; Initiator =$BF_3{\cdot}OEt_2$, PF_5, MeOTf, PhOTf, TMSOTf, TBDSOTf
c) bulk polymerization; Initiator = TMSOTf, [M]/[I] = 1000

Scheme 1.

Experimental

1,6-Anhydro-2,3,4-tri-*O*-allyl-β-D-glucopylanose (**2**) was prepared from 1,6-anhydro-2,3,4-tri-*O*-acetyl-β-D-glucopylanose[7,8] (**1**) by the treatment with allyl bromide in toluene in the presence of tetrabuthylammonium hydrogensulfate and sodium hydroxide powder at room temperature for 2 days in 90.7 % yield.

Solution and bulk polymerizations were carried out in an M-BRAUN stainless steel glove box equipped with gas purification system (molecular sieves and copper catalyst) under dry argon atmosphere. The moisture and oxygen contents (H_2O, O_2 > 1 ppm) in the glove box were monitored by an MB-MO-SE-1 and an MB-OX-SE-1 analyzers, respectively. Monomer **2** (3.7 g, 13.1mmol) was placed in a glass vial with screw cap under an argon atmosphere and TMSOTf (2.2 μl) was added by a microsyringe at -15 °C. After 100 h at -15 °C, the reaction mixture was poured into a large amount of methanol (c.a 500 mL). The methanol solution was evaporated under reduced pressure and then

the residue was purified by reprecipitation from chloroform/*n*-hexane to obtain 2,3,4-tri-*O*-allyl-(1→6)-α-D-glucopyranan (**3**).

Results and Discussion

We studied the cationic ring-opening polymerization of 1,6-anhydro-2,3,4-tri-*O*-allyl-β-D-glucopyranose (**2**) using various cationic initiators. Table 1 lists the results of the polymerization of **2** using Lewis acids, such as BF_3•OEt_2 and PF_5 in CH_2Cl_2. For the polymerization using BF_3•OEt_2 (**I**) for 24 h with a ratio [**M**]/[**I**] = 20, only trace of polymer was formed. However, when the amount of the initiator and the polymerization time increased, polymer yields increased and the obtained polymers were soluble in CH_2Cl_2, $CHCl_3$ and toluene and insoluble in hexane and methanol. The weight-average molecular weight (M_w) of the resulting polymers was determined using the static light scattering measurement (SLS). The maximum yield and M_w were 79 % and 215,600, respectively. PF_5 was used as a strong Lewis acid for the polymerization of 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-glucopyranose, which was required the high vacuum polymerization technique. Although the polymerization of **2** using PF_5 was performed under the high vacuum condition, the yield and M_w of the obtained polymers were lower than those for BF_3•OEt_2.

Table 1. Ring-opening polymerization using Lewis acids in CH_2Cl_2.

Initiator (**I**)	[**M**] mol•L^{-1}	[**M**]/[**I**]	T °C	t h	Yield[a] %	M_w g• mol^{-1}	M_w/M_n[b]
BF_3•OEt_2	2.0	50	-15	96	50	129,600	2.52
	2.0	10	-15	168	72	169,900	2.99
PF_5	3.5	50	-30	24	39	90,800	1.63
	3.5	10	-78	48	54	91,000	1.73

[a] *n*-Hexane-insoluble part.
[b] The M_w values were determined by static laser light scattering in $CHCl_3$ at 25 °C and the M_w/M_n values were determined by GPC in $CHCl_3$.

Alkyl and silyl trifluoromethanesulfonates were examined as new types of cationic initiators for the ring-opening polymerization of **2** (Table 2). For the alkyl triflates, $CF_3SO_3CH_3$ (MeOTf) exhibited lower initiating activity and a trace of polymer was obtained with $CF_3SO_3C_6H_5$ (PhOTf). On the other hand, the initiating activity of silyl triflates, $CF_3SO_3Si(CH_3)_3$ (TMSOTf) and $CF_3SO_3Si(CH_3)_2C(CH_3)_3$ (TBDSOTf), was extremely higher than that of the the alkyl triflates, e.g., the M_w values were relatively high as 58,700 ~ 104,900 and the values of M_w/M_ns were smaller those for BF_3•OEt_2.

Table 2. Ring-opening polymerization of **2** using alkyl and silyl trifluoromethane sulfonates in CH_2Cl_2.[a)]

Initiator (**I**)	[**M**]/[**I**]	t / h	Yield[b)] / %	M_w / g• mol^{-1}	M_w/M_n [c)]	$[\alpha]_D$ [d)]
MeOTf	20	80	25	63,700	1.18	+166.8°
	5	80	10	61,900	1.15	+166.3°
PhOTf	10	90	trace	-	-	-
	5	90	trace	-	-	-
TMSOTf	50	80	30	58,700	1.22	+165.1°
	10	80	75	104,900	1.70	+160.1°
TBDSOTf	50	80	50	86,300	1.89	+166.4°
	10	80	65	93,900	2.00	+161.1°

[a)] [**M**] = 2.0 mol•L^{-1}.
[b)] *n*-Hexane-insoluble part.
[c)] See Table1.
[d)] Measured in $CHCl_3$ at 25 °C (*c* 1.0).

In order to study the living characteristic of the cationic ring-opening polymerization initiated by TMSOTf, the bulk polymerization of **2** was carried out under the conditions of [**2**]/[TMSOTf] = 1000 at -15 and 22 °C.

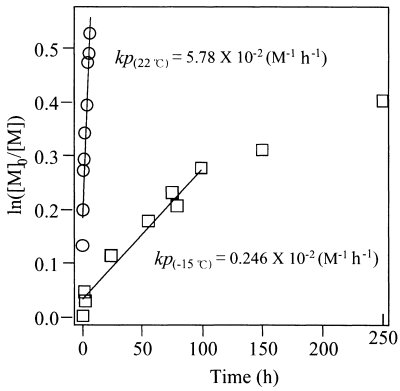


Figure 1. Plot of ln([M]$_0$/[M]) *vs.* time for the bulk cationic ring-opening polymerization of **2** using TMSOTf, [**M**]/[**I**] = 1000, Temperature: -15 °C (□), 22 °C (○).

Figure 1 shows the first-order plot of the polymerization of **2**. The rate of polymerization was strongly dependent on temperature. The polymerization rate constants (k_ps) for the polymerizations at -15 and 22 °C, which were estimated as the slope of the approximated line, were 0.246 × 10^{-2} $M^{-1}h^{-1}$ and 5.78 × 10^{-2} $M^{-1}h^{-1}$, respectively. A satisfactory linear relationship between ln([M]$_0$/[M]) and the polymerization time until 100 h was obtained at -15 °C.

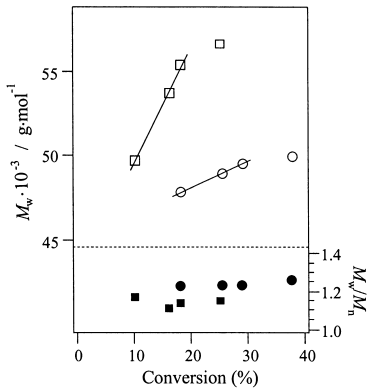


Figure 2. Dependence of $M_{w,SLS}$ and M_w/M_n on conversion for the bulk cationic ring-opening polymerization of **2** using TMSOTf, [**M**]/[**I**] = 1000, Temperature: -15 °C (□,■), 22 °C (O,●).

Figure 2 shows the plots of the M_w *vs.* conversion. For the polymerization of **2** at -15 °C, the M_w linearly increased in proportion to conversion and went up to 56,600 at 25 % conversion and the M_w/M_n values were very low as 1.11 ~ 1.17, indicating that the control of the molecular weight and M_w/M_n were possible in the case of low temperature. On the other hand, in the case of the polymerization at 22 °C, the M_w and M_w/M_n were 47,800 ~ 49,500 and ca. 1.2, respectively, so that the polymerization control was somewhat difficult in higher temperature. These results indicated that the initiator, TMSOTf, promoted the "living" cationic ring-opening polymerization of **2** at low temperature.

In the ^{13}C NMR spectrum of the obtained polymer using TMSOTf, as shown in Figure 3, the signals at 74.49 – 71.73, 118.04 – 117.62 and 135.96 –135.59 ppm were assigned to the O–CH_2–, =CH_2, –CH=, and of the allyl group, respectively, and those at 81.61, 79.93, 77.55, 71.11, and 65.99 ppm were assigned to the C2', C3', C4', C5', and C6' of the glucose unit. In addition, that signal at 101.10 ppm due to the β-configuration of the anomeric carbon (C1) for **2** disappeared, and the single at 97.66 ppm (C1') was observed. The change in the anomeric carbon from monomer to polymer was observed for the cationic ring-opening polymerization of trimethyl and triethyl 1,6-anhydro sugars, indicating that the cationic polymerization of **2** regioselectively proceeded to give the highly stereoregulated polymer,
i.e., 2,3,4-tri-*O*-allyl-(1→6)-α-D-glucopyranan (**3**).

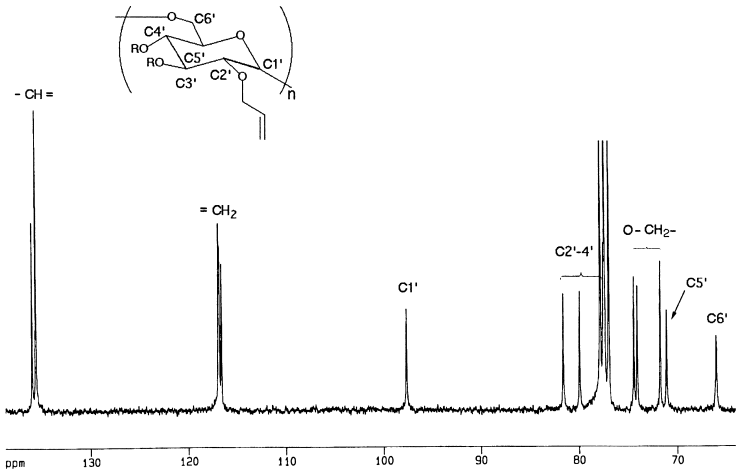


Figure 3. ^{13}C NMR spectrum of 2,3,4-tri-*O*-allyl-(1→6)-α-D-glucopyranan (**3**).

Conclusions

We have demonstrated the new synthetic method of well-defined polysaccharide by the "living" cationic ring-opening polymerization of **2**. Excellent control of the molecular weight and molecular weight distribution of the resulting polymer was achieved through the bulk polymerization using TMSOTf as an initiator. A further investigation of the "living" polymerization is now in progress in terms of the end-functionalized polymer such as a polysaccharide macromonomer. In addition, the method using the allyl ether linkage as the hydroxyl protecting group could be applied to produce other polysaccharides through the ring-opening polymerization of anhydro sugars.

[1] C. Schuerch, *"Advances in Carbohydrate Chemistry and Biochemistry"*, Academic Press, New York 1973.
[2] T. Uryu, K. Hatanaka, Y. Sakamoto, K. Harima, A. Hagino, K. Ito, A. Funamoto, K. Matsuzaki, *Nippon Kagaku Kaishi* **1982**, *10*, 1638.
[3] T. Uryu, C. Schuerch, *Macromolecules* **1971**, *4*, 342.
[4] J. Zachoval, C. Schuerch, *J. Am. Chem. Soc.* **1969**, *91*, 1165.
[5] T. Kakuchi, A. Kusuno, M. Miura, H. Kaga, *Macromol. Rapid Commun.* **2000**, *21*, 1003.
[6] A. Kusuno, M. Mori, M. Miura, H. Kaga, T. Kakuchi, *Enantiomer* **2001**, *6*, 27.
[7] M. Miura, H. Kaga, S. Tanaka, K. Takahashi, K. Ando. *J. Chem. Eng. Japan* **2000**, *33*, 299.
[8] M. Miura, H. Kaga, T. Yoshida, K. Ando, *J. Wood Sci.* **2001**, *47*, 502.