

## Ring-opening polymerization of new 1,6-anhydro- $\beta$ -D-glucosamine derivatives

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Received 26 September 1997; revised 20 January 1998; accepted 21 January 1998

### Abstract

New 1,6-anhydro-glucosamine monomers having amino protecting groups at C2 positions; i.e. 1,6-anhydro-3,4-di-*O*-benzyl-2-(*N,N*-cyclo(1,2-bis(dimethylsilyl)ethylamino)-2-deoxy- $\beta$ -D-glucopyranose (A2NSG), 1,6-anhydro-3,4-di-*O*-benzyl-2-hexamethyleneimino-2-deoxy- $\beta$ -D-glucopyranose (A2NHG) and 1,6-anhydro-3,4-di-*O*-benzyl-2-(*N,N*-dibenzylamino)-2-deoxy- $\beta$ -D-glucopyranose (A2NBG), were synthesized in order to investigate the effects of the 2-amino groups on cationic ring-opening polymerizations. When phosphorus pentafluoride and antimony pentachloride were used as initiators, the A2NSG monomer gave polymers having number-average molecular weights of  $\bar{M}_n = 4.1 \times 10^3$  and  $3.4 \times 10^3$  ( $\bar{P}D_n = 13$  and 8), respectively. The resulting polymers had positive specific rotations ranging from  $[\alpha]_D^{25} = +33.1^\circ$  to  $+44.1^\circ$  and the Cl signal in the  $^{13}\text{C}$  NMR spectra appeared as a single peak around 100 ppm, which suggested that the polymers had 1,6- $\alpha$  stereoregularity. The A2NHG monomer gave polymers in low yields, and the A2NBG monomer had no polymerizability. These results suggest that the ring-opening polymerization of 1,6-anhydro-glucosamine monomers depends on both electron withdrawal and steric hindrance of the 2-amino protecting groups. © 1998 Elsevier Science Ltd. All rights reserved

**Keywords:** Polymerization; 1,6-anhydro- $\beta$ -D-glucosamine; Ring-opening

### 1. Introduction

2-Amino-2-deoxy-D-glucopyranose (D-glucosamine) is a component of heparin, a sulfated mucopolysaccharide having strong blood anticoagulant activity (Björk and Lindahl, 1982), of chitin and chitosan (Murata et al., 1991; Okamoto et al., 1993), and of many antibiotics, and so it plays important roles in specific biological activities. Chemical synthesis of amino polysaccharides with well-defined structures and molecular weights is important to elucidate the relationship between biological functions and structures of natural polysaccharides as well as to develop a new biological active material having anti-HIV activity (Uryu et al., 1996).

Polymerization of 1,6-anhydro-glucopyranose having an amide group affords only oligomers and the amide group is not a suitable protective group for an amino group (Uryu et al., 1982). An azido group, a precursor of an amino group, is stable in the cationic ring-opening polymerization, as was reported previously for the ring-opening polymerizations of 1,6-anhydro-glucopyranose derivatives having azido groups

at the C2, C3 or C4 position (Uryu et al., 1983). Although the 3-azido monomer gave a polymer having high molecular weights, both 2- and 4-azido monomers afforded only oligomers. An amino-group-containing polysaccharide prepared by the reduction of the 3-azido group was sulfated to give an sulfamide-group-containing glucopyranan. The sulfated 3-amino-(1  $\rightarrow$  6)- $\alpha$ -D-glucopyranan had a high blood anticoagulant activity, but low toxicity (Hatanaka et al., 1987). Further, ring-opening polymerization of anhydro-ribose (Kang et al., 1997), xylose (Yoshida et al., 1996), and allose (Hattori et al., 1997) derivatives having azido groups at the C3 positions gave stereoregular polysaccharides having amino groups at the C3 positions in the sugar units. 1,6-Anhydro-3,4-di-*O*-benzyl-2-deoxy-2-phthalimido- $\beta$ -D-glucopyranose was polymerized with the aid of  $\text{PF}_5$  catalyst to give glucosamine oligomers having degrees of polymerization of 5–7 (Kanno et al., 1995).

Amino-group-containing polysaccharides consisting of an  $\alpha$ -D-glucosamine unit in which the amino group is located at the C2 position have not been synthesized by ring-opening polymerization of anhydro-sugar derivatives, because anhydro-sugar monomers having a 2-azido group have a low polymerizability. In this paper, we report synthesis and

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ring-opening polymerizations of new 1,6-anhydro-glucosamine derivatives having di-*O*-benzyl and cyclic amino protecting groups to give (1 → 6)- $\alpha$ -D-glucopyranan derivatives having 2-amino groups in the sugar units. The polymers structure are determined by specific rotations and high-resolution NMR spectroscopy.

## 2. Materials and methods

### 2.1. General

Melting points were determined by means of a Shibata MEL-270 apparatus and were uncorrected. 400 MHz  $^1\text{H}$  and 100 MHz  $^{13}\text{C}$  NMR spectra were recorded on a JEOL JNM  $\alpha$ -400 spectrometer in  $\text{CDCl}_3$  with tetramethylsilane as an internal standard. All the data sizes for DQF-COSY (double quantum filtered correlation spectroscopy), HMQC (heteronuclear multiple quantum coherence) and HMBC (heteronuclear multiple bonds connectivity) measurements were 512 (t2)  $\times$  256 (t1) points with a pulsed field gradient, and two-fold zerofilling was carried out along the f1 axis to give two-dimensional spectra with 512  $\times$  512 points. In the HMBC experiments, mixing time ( $\tau_m$ ) of 50 ms and delay time of 1.5 s were used. Infrared spectra were obtained with JASCO IR-700 spectrometer using the KBr pellet method. Purification of monomers were performed by means of a preparative HPLC using silica-gel column of 21.5  $\times$  300 mm (TOSO TSK-gel, silica-60) eluted with hexane–ethyl acetate solvent system. Specific rotations were measured in chloroform with a JASCO DIP-140 digital polarimeter. Molecular weights of polymers were estimated by means of gel-permeation chromatography (columns; TOSO TSK-gel G3000H<sub>XL</sub>, G4000H<sub>XL</sub>, and G5000H<sub>XL</sub>, 7.6 mm  $\times$  300 mm  $\times$  3; eluent, tetrahydrofuran) using polystyrene standards.

### 2.2. Monomer synthesis

#### 2.2.1. 2-amino-1,6-anhydro-3,4-di-*O*-benzyl-2-deoxy- $\beta$ -D-glucopyranose (3)

Lithium aluminum hydride (0.380 g, 10.0 mmol) in dry tetrahydrofuran (10 ml) was added slowly to a solution of 1,6-anhydro-2-azido-3,4-di-*O*-benzyl-2-deoxy- $\beta$ -D-glucopyranose (2) (3.67 g, 10.0 mmol) in dry tetrahydrofuran (50 ml) under nitrogen atmosphere at 0°C and then the mixture was stirred for 0.5 h at room temperature. After methanol (5 ml) was added to the mixture, the solvents were evaporated to dryness. The residue was dissolved in chloroform (50 ml) and poured into a stirred aqueous solution saturated with potassium sodium tartrate (200 ml). The chloroform layer was washed with water, dried over anhydrous sodium sulfate, and concentrated for chromatography on silica-gel. Elution of the column with ethyl acetate/methanol = 4/1 (volume ratio) afforded 2-amino-1,6-anhydro-3,4-di-*O*-benzyl-2-deoxy- $\beta$ -D-glucopyranose (3) (3.24 g) in 95% yield as syrup. The

ninhydrin test was positive. Specific rotation  $[\alpha]_D^{25} = -46.9^\circ$  (c1,  $\text{CHCl}_3$ ). IR (chloroform);  $\nu = 3368\text{ cm}^{-1}$  ( $-\text{NH}_2$ ).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ );  $\delta$  2.01 (br, 2H,  $\text{NH}_2$ ), 3.36 (s, 1H, H3), 3.56 (s, 1H, H4), 3.70–3.73 (t, 1H, H6<sub>exo</sub>), 4.12–4.14 (H6<sub>endo</sub>), 4.45–4.61 (m, 5H, 2  $\times$   $\text{PhCH}_2$ -, H5), 5.40 (s, 1H, H1), 7.27–7.35 ppm (m, 10H, phenyl).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ );  $\delta$  51.7 (C2), 65.0 (C6), 71.1, 71.8 (2  $\times$   $\text{PhCH}_2$ -), 74.0 (C5), 75.6 (C3), 78.3 (C4), 103.3 (C1), 127.6–137.9 ppm (phenyl).

#### 2.2.2. 1,6-anhydro-3,4-di-*O*-benzyl-2-(*N,N*-cyclo(1,2-bis(dimethylsilyl)ethylamino)-2-deoxy- $\beta$ -D-glucopyranose (4) (A2NSG)

*n*-Butyllithium in hexane (1.71 mol/l, 3.5 ml) was added from a syringe to a stirred solution of 3 (1.71 g, 5.0 mmol) in dry tetrahydrofuran (THF) (15 ml) under nitrogen at  $-78^\circ\text{C}$ . 1,2-Bis(dimethylchlorosilyl)ethane (1.29 g, 6.0 mmol) in THF (5 ml) was added dropwise to the mixture, and stirring was continued for 1 h. After methanol (1 ml) was added, the mixture was allowed to warm at room temperature and poured into water. After evaporation, the residue was dissolved in chloroform (50 ml) and then washed with water, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by silica-gel chromatography, followed by preparative HPLC (column: 21.5  $\times$  300 mm, hexane/ethyl acetate = 4/1 (volume ratio) with 0.1% triethylamine as eluent) to give an 1,6-anhydro-3,4-di-*O*-benzyl-2-(*N,N*-cyclo(1,2-bis(dimethylsilyl)ethylamino)-2-deoxy- $\beta$ -D-glucopyranose (4) (A2NSG) (1.89 g) in 89.9% yield as a colorless syrup. Specific rotation  $[\alpha]_D^{25} = -76.1^\circ$  (c1,  $\text{CHCl}_3$ ). IR (chloroform);  $\nu = 1251\text{ cm}^{-1}$  (Si–C).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ );  $\delta$  0.14–0.15 (d, 12H,  $-\text{Si-CH}_3$ ), 0.71–0.76 (q, 4H,  $-\text{Si-CH}_2$ -), 2.96–2.97 (d, 1H, H2), 3.40–3.41 (t, 1H, H4), 3.56–3.67 (m, 3H, H3), 4.51–4.52 (d, 1H, H5), 4.56–4.64 (q, 2H, C4- $\text{PhCH}_2$ -), 4.62–4.73 (q, 2H, C3- $\text{PhCH}_2$ -), 5.19 (s, 1H, H1), 7.25–7.34 ppm (m, 10H, phenyl).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ );  $\delta$  0.9, 1.3 ( $-\text{Si-CH}_3$ ), 8.3 ( $-\text{Si-CH}_2$ -), 60.3 (C2), 67.4 (C6), 71.6 (C4- $\text{PhCH}_2$ -), 73.4 (C3- $\text{PhCH}_2$ -), 75.5 (C5), 81.8 (C3), 83.6 (C4), 106.8 (C1), 127.4–138.8 ppm (phenyl). Anal. calcd for  $\text{C}_{26}\text{H}_{37}\text{NO}_4\text{Si}_2$ : C, 64.55; H, 7.71; N, 2.90. Found: C, 64.28; H, 7.70; N, 3.03.

#### 2.2.3. 1,6-anhydro-3,4-di-*O*-benzyl-2-hexamethyleneimino-2-deoxy- $\beta$ -D-glucopyranose (5) (A2NHG)

*n*-Butyllithium in hexane (1.71 mol/l, 3.5 ml) was added to a solution of 3 (1.71 g, 5.0 mmol) in THF (200 ml) under nitrogen at  $-78^\circ\text{C}$ , and the mixture was stirred for 0.5 h. 1,6-Dibromohexane (2.3 ml, 15 mmol) was added dropwise to the mixture and stirred for 10 h. After addition of methanol (1 ml) and removal of the solvent by evaporation, the residue was dissolved in chloroform (50 ml). The chloroform solution was washed with water, dried over anhydrous sodium sulfate, and evaporated. The crude product was

Table 1  
Ring-opening polymerization of 1,6-anhydro-glucosamine derivatives<sup>a</sup>

| No.            | Monomer | Catalyst          | mol%  | CH <sub>2</sub> Cl <sub>2</sub> (ml) | Time (h) | Yield % | $\bar{M}_n^b \times 10^3$ | $[\alpha]_D^{25c}$ (deg) |
|----------------|---------|-------------------|-------|--------------------------------------|----------|---------|---------------------------|--------------------------|
| 1 <sup>d</sup> | A2NSG   | PF <sub>5</sub>   | 5.0   | 0.2                                  | 12       | 5       | 1.3                       | + 44.1                   |
| 2              |         | PF <sub>5</sub>   | 10.0  | 0.2                                  | 12       | 34      | 4.1                       | + 33.1                   |
| 3              |         | PF <sub>5</sub>   | 10.0  | 0.2                                  | 24       | 28      | 2.6                       | + 34.0                   |
| 4              |         | SbCl <sub>5</sub> | 10.0  | 0.2                                  | 24       | 12      | 1.8                       | + 35.5                   |
| 5 <sup>d</sup> | A2NHG   | SbCl <sub>5</sub> | 10.0  | 0.4                                  | 8        | 15      | 2.3                       | + 39.8                   |
| 6              |         | PF <sub>5</sub>   | 10.0  | 0.2                                  | 24       | 8       | 2.6                       | —                        |
| 7              |         | PF <sub>5</sub>   | 10.0  | 0.4                                  | 24       | 12      | 3.3                       | + 59.3                   |
| 8              |         | PF <sub>5</sub>   | 10.0  | 0.4                                  | 48       | 17      | 3.4                       | + 55.4                   |
| 9              | A2NBG   | PF <sub>5</sub>   | 10.0  | 0.2                                  | 24       | —       | —                         | —                        |
| 10             |         | PF <sub>5</sub>   | 10.0  | 0.4                                  | 48       | 5       | 1.8                       | —                        |
| 11             |         | PF <sub>5</sub>   | 20.0  | 0.2                                  | 48       | —       | —                         | —                        |
| 12             |         | PF <sub>5</sub>   | 100.0 | 0.2                                  | 72       | 3       | —                         | —                        |

<sup>a</sup>Monomer; 0.200 g, temp: – 60°C.

<sup>b</sup>Determined by GPC.

<sup>c</sup>Measured in CHCl<sub>3</sub> (c.1).

<sup>d</sup>Temp: – 40°C.

successively chromatographed on silica-gel and the preparative HPLC [hexane ethyl acetate = 2/1 (volume ratio)] to afford 1,6-anhydro-3,4-di-*O*-benzyl-2-hexamethyleneimino-2-deoxy-β-D-glucopyranose (**5**) (A2NHG) (0.67 g) in 31% yield as a colorless syrup. Specific rotation  $[\alpha]_D^{25} = -59.4^\circ$  (c1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (CDCl<sub>3</sub>); δ 1.57–1.61 (m, 8H, Hb and Hc), 2.69–2.70 (d, 1H, H2), 2.76–2.90 (m, 4H, Ha), 3.40–3.41 (d, 1H, H4), 3.56–3.58 (t, 1H, H3), 3.62–3.66 (t, 1H, H6exo), 3.72–3.74 (d, 1H, H6endo), 4.52–4.54 (d, 1H, H5), 4.55–4.63 (q, 2H, C4-PhCH<sub>2</sub>), 4.62–4.79 (q, 2H, C3-PhCH<sub>2</sub>), 5.45 (s, 1H, H1), 7.26–7.37 ppm (m, 10H, phenyl). <sup>13</sup>C NMR (CDCl<sub>3</sub>); δ 27.0 (Cc), 30.1 (Cb), 52.2 (Ca), 66.1 (C6), 69.9 (C2), 71.5 (C3-PhCH<sub>2</sub>), 72.7 (C4-Ph-CH<sub>2</sub>), 75.1 (C5), 77.1 (C3), 81.6 (C4), 101.6 (C1), 127.6–138.6 ppm (phenyl). Anal. calcd for C<sub>26</sub>H<sub>33</sub>NO<sub>4</sub>: C, 73.73; H, 7.85; N, 3.31. Found: C, 73.60; H, 7.80; N, 3.29.

#### 2.2.4. 1,6-anhydro-3,4-di-*O*-benzyl-2-(*N,N*-dibenzylamino)-2-deoxy-β-D-glucopyranose (**6**) (A2NBG)

Benzyl bromide (1.8 ml, 15 mmol) was added dropwise to a dry *N,N*-dimethylformamide (DMF) (20 ml) solution of **3** (1.71 g, 5.0 mmol) and sodium hydride (1.0 g, 60% in oil which was washed with hexane several times), and the mixture was stirred for 24 h at 50°C. After addition of methanol (1 ml) and chloroform (50 ml), the chloroform layer was washed with water. The separated water layer was further extracted with chloroform (20 ml) three times. The combined chloroform layer was dried over anhydrous sodium sulfate and concentrated to give a crude crystal, which was recrystallized from ethanol three times and then finally from *n*-butyl chloride to give 1,6-anhydro-3,4-di-*O*-benzyl-2-(*N,N*-dibenzylamino)-2-deoxy-β-D-glucopyranose (**6**) (A2NBG) (2.04 g) in 78% yield as a white crystal. Specific rotation  $[\alpha]_D^{25} = -38.4^\circ$  (c1, CHCl<sub>3</sub>). m.p. 123.5–125.0°C.

<sup>1</sup>H NMR (CDCl<sub>3</sub>); δ 2.86–2.87 (d, 1H, H2), 3.39 (s, 1H, H4), 3.63–3.66 (q, 1H, H6exo), 3.70 (s, 1H, H3), 3.76–3.91 (q, 4H, 2 × PhCH<sub>2</sub>-N), 3.79–3.81 (t, 1H, H6endo), 4.34–4.42 (q, 2H, C3-PhCH<sub>2</sub>-), 4.48–4.55 (q, 2H, C4-PhCH<sub>2</sub>-), 4.57–4.59 (d, 1H, H5), 5.68 (s, 1H, H1), 7.19–7.38 ppm (m, 20H, Phenyl). <sup>13</sup>C NMR (CDCl<sub>3</sub>); δ 54.9 (2 × PhCH<sub>2</sub>-N), 60.6 (C2), 65.1 (C6), 71.1 (C4-Ph-CH<sub>2</sub>-), 71.4 (C3-PhCH<sub>2</sub>-), 74.5 (C5), 76.7 (C3), 79.3 (C4), 100.6 (C1), 126.9–139.9 ppm (phenyl). Anal. calcd for C<sub>34</sub>H<sub>35</sub>NO<sub>4</sub>: C, 78.28; H, 6.76; N, 2.69. Found: C, 78.08; H, 6.78; N, 2.71.

#### 2.3. Polymerization

All the polymerizations were carried out under high vacuum (~10<sup>-6</sup> mmHg) in a sealed glass ampoule with branches of catalyst and solvent tubes which were prepared under the same high vacuum before attaching (Ruckel and Schuerch, 1966; Uryu et al., 1977). Typical procedure is as follows: Under nitrogen, A2NSG (0.200 g, 0.04 mmol) was introduced into the ampoule and then kept overnight under high vacuum (~10<sup>-6</sup> mmHg). After freezing the ampoule with liquid nitrogen, methylene chloride (0.2 ml) and catalyst (10 mol% to monomer) were moved successively from the tubes through the adjoining breakseals. Phosphorus pentachloride was introduced into the ampoule by decomposition of *p*-chlorobenzenediazonium hexafluorophosphate with flame of gas. SbCl<sub>5</sub> catalyst was moved directly to the ampoule cooled by liquid nitrogen. After melting off the branches, the ampoule was cut off from the vacuum line and then the polymerization was started at – 60°C.

After 12 h, the polymerization was terminated by addition of methanol and the product was dissolved in chloroform. The chloroform layer was washed with water several times, dried over anhydrous sodium sulfate, and concentrated. The resulting polymer was purified by

reprecipitation using chloroform–petroleum ether three times and isolated by freeze-drying from benzene to give white powder in 34% yield.  $\bar{M}_n = 3.4 \times 10^3$  ( $\bar{P}D_n = 8$ ) (no. 2 in Table 1).

### 3. Results and discussion

#### 3.1. Monomer synthesis

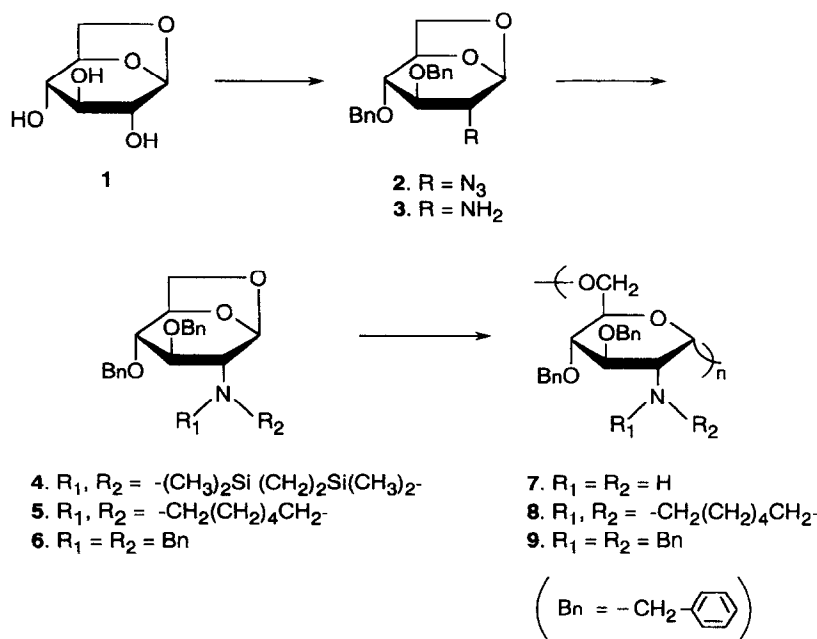
1,6-Anhydro-2-azido-3,4-di-*O*-benzyl-2-deoxy- $\beta$ -D-glucopyranose (**2**) was synthesized from 1,6-anhydro- $\beta$ -D-glucopyranose (**1**) in several steps according to the method of Paulsen and Stenzel (1978). If this 2-azido monomer is polymerized, polysaccharides having amino groups at C2 positions in the sugar units will be obtained via conversion of the azido groups into amino groups. However, we reported previously that this azido monomer **2** had extremely low cationic ring-opening polymerizability because of an intramolecular interaction of the azido group at C2 position with the C1 carbon at the propagating cationic end (Uryu et al., 1983). Therefore, in this study, we intended to prepare polymerizable anhydro sugar monomers containing protected amino groups, which are converted from an azido group as shown in Scheme 1. Reduction of **2** with lithium aluminum hydride gave 2-amino-1,6-anhydro-3,4-di-*O*-benzyl-2-deoxy- $\beta$ -D-glucopyranose (**3**) in good yield without any side-reactions. Although acyl groups are generally used as amino protecting groups, the acyl groups are not suitable for the cationic ring-opening polymerization by reason that Lewis acid catalysts are sensitive to both carbonyl group and remaining amino proton. Therefore, cyclic protecting groups were used to protect both amino protons.

The protection of the amino group in **3** with 1,2-bis(dimethylchlorosilyl)ethane, 1,6-dibromohexane, and benzyl bromide, gave the three monomers, 1,6-anhydro-3,4-di-*O*-benzyl-2-(*N,N*-cyclo(1,2-bis(dimethylsilyl)ethylamino))-2-deoxy- $\beta$ -D-glucopyranose (A2NSG), 1,6-anhydro-3,4-di-*O*-benzyl-2-(hexamethyleneimino)-2-deoxy- $\beta$ -D-glucopyranose (A2NHG), and 1,6-anhydro-3,4-di-*O*-benzyl-2-deoxy-2-(*N,N*-dibenzylamino)- $\beta$ -D-glucopyranose (A2NBG), respectively. These monomers were purified by means of HPLC or recrystallization. Elemental analyses of monomers was in good agreement with the calculated values. They had the specific rotations of  $[\alpha]_D^{25} = -76.1^\circ$ ,  $-59.4^\circ$  and  $-38.4^\circ$ , respectively.

Fig. 1 shows the  $^1\text{H}$  MBR spectra of monomers, in which all signals were assigned by a combination of the pulsed field gradient DQF-COSY (double quantum filtered correlation spectroscopy), HMQC (heteronuclear multiple quantum coherence), and HNMC (heteronuclear multiple bonds connectivity) spectra. The H1 signals appeared at 5.19, 5.45 and 5.68 ppm for A2NSG, A2NHG and A2NBG, respectively, which suggested that the difference of the chemical shift depended on the electron-withdrawing strength of the amino protecting groups at C2 position.

#### 3.2. Polymerization

Ring-opening polymerizations of A2NSG, A2NHG and A2NBG were performed with Lewis acid catalysts such as phosphorus pentafluoride and antimony pentachloride in methylene chloride under high vacuum. The results of polymerizations are summarized in Table 1. The polymerization of A2NSG was firstly carried out at  $-40^\circ\text{C}$  with 5.0 mol%



Scheme 1. Synthetic route of 2-amino-3,4-di-*O*-benzyl-2-deoxy-(1  $\rightarrow$  6)- $\alpha$ -D-glucopyranan.

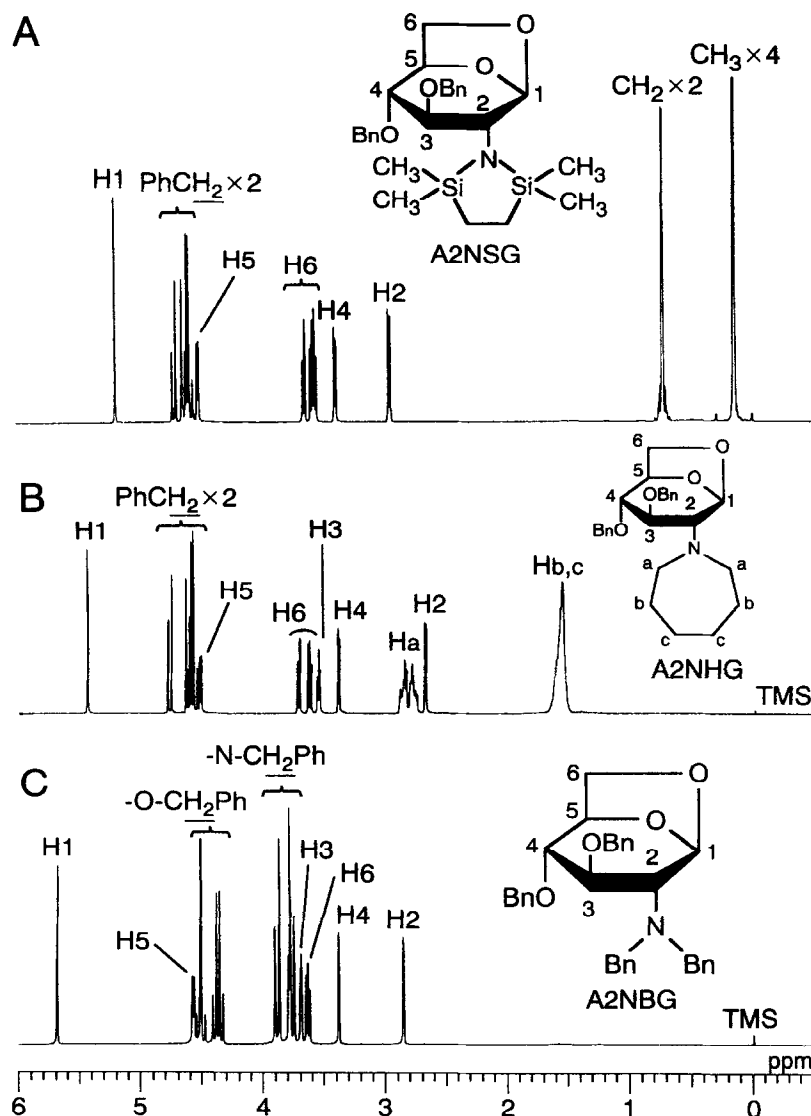


Fig. 1. 400 MHz  $^1\text{H}$  NMR spectra of: (a) 1,6-anhydro-3,4-di-*O*-benzyl-2-*(N,N*-cyclo(1,2-bis(dimethylsilyl)ethylamino)-2-deoxy- $\beta$ -D-glucopyranose (A2NSG); (b) 1,6-anhydro-3,4-di-*O*-benzyl-2-hexamethyleneimino-2-deoxy- $\beta$ -D-glucopyranose (A2NHG); (c) 1,6-anhydro-3,4-di-*O*-benzyl-2-deoxy-2-*(N,N*-dibenzylamino)- $\beta$ -D-glucopyranose (in  $\text{CDCl}_3$  as solvent).

of  $\text{PF}_5$  catalyst for 12 h. However, an oligomer ( $\bar{M}_n = 1.3 \times 10^3$ ,  $\bar{P}D_n = 4$ ) was obtained in a very low yield (5%).

With 10 mol% of  $\text{PF}_5$  at  $-60^\circ\text{C}$ , A2NSG was polymerized for 48 h into a polymer having a number-average molecular weight of  $4.1 \times 10^3$  ( $\bar{P}D_n = 13$ ) in 34% yield. By contrast,  $\text{SbCl}_5$  catalyst gave low molecular weight polymers in low yields. These polymers had positive specific rotations in the range of  $[\alpha]_D^{25} = +33.1$ – $+44.1^\circ$ , indicating that the polymers were composed of an 1,6- $\alpha$ -linked structure. A2NHG having cyclic alkylene amino protecting group afforded polymers with  $\text{PF}_5$  catalyst at  $-60^\circ\text{C}$  for long polymerization times, but the yields were low. Their number-average molecular weights were  $\bar{M}_n = 2.6 \times 10^3$  to  $3.4 \times 10^3$  ( $\bar{P}D_n = 6$  to 8), and the specific rotations were  $[\alpha]_D^{25} = +55.4^\circ$  and  $+59.3^\circ$ . A2NBG having the dibenzyl amino protecting group exhibited extremely low polymerizability with use of  $\text{PF}_5$  catalyst in the

range of 10–100 mol%. In the polymerization of A2NBG, the solution was changed from colorless to light red by addition of the  $\text{PF}_5$  catalyst, which suggested that complexation of the  $\text{PF}_5$  with the dibenzyl amino group.

The low polymerizability of the substituted amino-group-containing monomers might be attributed to: (1) high nucleophilicity of the nitrogen in the substituted amino groups; (2) high electron density of the nitrogen bonded to silicones having low electronegativity in the case of A2NSG; and (3) bulkiness of the wholly substituted amino groups.

According to (1) and (2), Lewis acid catalysts might tend to coordinate with the N2 nitrogen in addition to the O6 oxygen, and thereby the polymerizability was decreased. As for (3), Kobayashi et al. reported that a bulky axial substituent at the C2 position has large effects on the polymerizability of 1,6-anhydro sugars (Kobayashi and Schuerch,

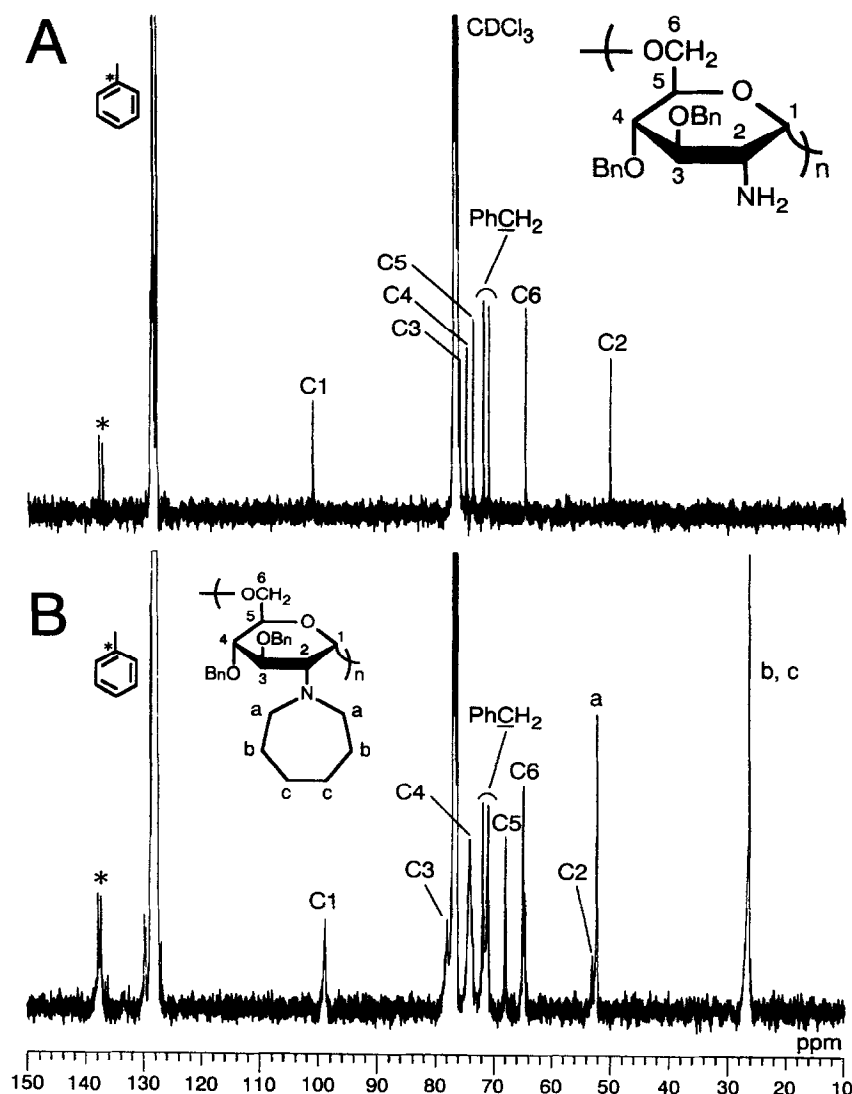


Fig. 2. 100 MHz  $^{13}\text{C}$  NMR spectra of: (a) 2-amino-3,4-di-*O*-benzyl-2-deoxy-(1  $\rightarrow$  6)- $\alpha$ -D-glucopyranan; and (b) 3,4-di-*O*-benzyl-2-hexamethyleneimino-2-deoxy-(1  $\rightarrow$  6)- $\alpha$ -D-glucopyranan (in  $\text{CDCl}_3$  as solvent).

1977). Accordingly, low conversions of A2NHG having a bulky substituent at the C2 position might be owing to the difficult approach of the monomer to a propagating end.

Although the A2NBG monomer substituted by electron-withdrawing benzyl groups must be electronically favorable for the ring-opening polymerization, it exhibited almost no polymerizability. The reason for the low reactivity is assumed to be large steric hindrance originating from the bulky *N,N*-dibenzylamino group. Previously, it was reported that such 1,6-anhydro-disaccharides as 1,6-anhydro-maltose and -cellobiose derivatives, which can be regarded as bulky substituted 1,6-anhydro-glucose derivatives, had low polymerizabilities (Veruovic and Schuerch, 1970; Masura and Schuerch, 1970).

The electron withdrawing effects of the amino-protecting groups at C2 position could be observed from the NMR chemical shift of H1 protons, as shown in Fig. 1. The H1 signals appeared at 5.19, 5.45 and 5.68 ppm for A2NSG,

A2NHG, and A2NBG probably in the order of the electron withdrawing property of the C2 substituent.

### 3.3. $^{13}\text{C}$ NMR spectra of polymers

Fig. 2 shows  $^{13}\text{C}$  NMR spectra of: (a) 2-amino-3,4-di-*O*-benzyl-2-deoxy-(1  $\rightarrow$  6)- $\alpha$ -D-glucopyranan having  $[\alpha]_D^{25} = +33.1^\circ$ ; and (b) 3,4-di-*O*-benzyl-2-hexamethyleneimino-2-deoxy-(1  $\rightarrow$  6)- $\alpha$ -D-glucopyranan having  $[\alpha]_D^{25} = +55.4^\circ$ , in which all signals were assigned in combination with DQF-COSY, HMQC, and HMBC spectra. The C1 signals appeared around 100 ppm in both spectra as a single peak, suggesting high stereoregularity. Taking into account the positive specific rotations and the  $^{13}\text{C}$  NMR spectra, these polymers had 1,6- $\alpha$  stereoregularity. In spectrum A, the polymer obtained from A2NSG had free amino groups, but no silyl groups. In the IR spectrum, the Si–C stretching vibration at  $1250\text{ cm}^{-1}$  disappeared, with N–H stretching vibration owing to amino groups appearing. Since silyl

protecting groups such as *tert*-butyldimethylsilyl and trimethylsilyl groups were easily deprotected by fluoride ions, the cyclic silyl protecting group of A2NSG was assumed to be deprotected during the polymerization by PF5 catalyst. This side reaction might be the reason for the low polymerizability.

After debenzoylation of polymer **7**, the resulting polysaccharides having free amino groups at the C2 position can be a good model compounds to elucidate the specific biological activities or natural and artificial amino polysaccharides.

### Acknowledgements

This work was partially supported by a Research Fellowship of the Japan Society for the Promotion of Science for Young Scientists (K.H.).

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