Polymerization of 6-Amino-6-deoxy-D-glucose Involving Amadori Rearrangement: A New Method for Synthesis of Aminopolysaccharide

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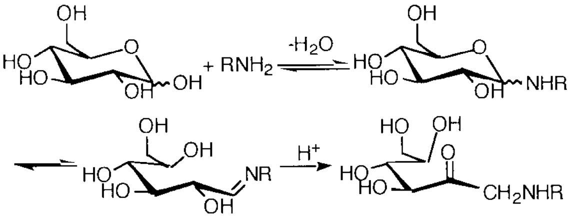
This paper describes synthesis of a new aminopolysaccharide by thermal polymerization of 6-amino-6-deoxy-D-glucose in the presence of acetic acid. The polymerization proceeded via Amadori rearrangement to give the aminopolysaccharide having aminoketose structure in the main chain. The molecular weight was determined by GPC analysis after acetylation of the product polysaccharide.

Aminopolysaccharides have attracted much attention because of their unique structures and properties which are generally different from those of normal polysaccharides such as cellulose. For example, chitin is the most abundant aminopolysaccharide among the naturally occurring polysaccharides and has been of great interest in numerous scientific and application fields.[1]

Synthesis of aminopolysaccharides, therefore, is one of the important research projects to elucidate the biological mechanism of naturally occurring aminopolysaccharides. A few methods, however, such as the ring-opening polymerization,[2] enzymatic polymerization,[3] and glycosylation[4] have been developed to synthesize aminopolysaccharides with well-defined structures.

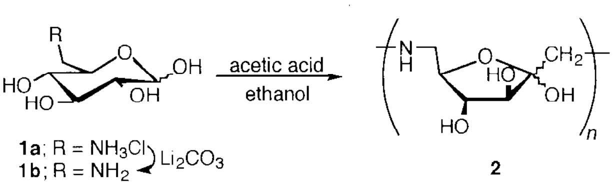
On the other hand, a specific reaction between saccharide and amine under acidic condition has been well-known as Amadori rearrangement to form aminoketose.[5] The mechanism of the reaction has been considered as follows (Scheme 1); glycosylamine, which is formed by the condensation of saccharide with amine, is converted into Schiff base structure, followed by the rearrangement to give aminoketose. Moreover, the chain form of the aminoketose may be in equilibrium with the ring structure.



Scheme 1.

In this communication, we report polymerization of 6-amino-6-deoxy-D-glucose (**1b**) under acidic condition via Amadori rearrangement to give new aminopolysaccharide (**2**) (Scheme 2). However, **1b** is not stable in a free base form especially in solution, and thus its hydrochloride (**1a**) was used as a monomer.

A typical example was as follows (entry 2). Under argon, a mixture of monomer **1a**[6] (2.81 mmol, 0.603 g) and lithium carbonate (1.41 mmol, 0.104 g) as an acid acceptor was stirred in ethanol (8.0 mL) for 1 h at room temperature. Then, to a mixture was added acetic acid (2.81 mmol, 0.169 g) and the solution was refluxed for 3 h. After cooling the mixture, the precipitated product was isolated by filtration and dried in vacuo to give polysaccharide **2** (1.97 mmol, 0.318 g) in 70.2 % yield. The structure of the product polymer was determined by ^{1}H NMR, ^{13}C NMR, and IR spectra. Figure 1b shows the ^{1}H NMR spectrum of the product (D_2O) in comparison with that of **1a** in Figure 1a. The peaks due to an anomeric proton of **1a** completely disappears in the spectrum of the product, indicating that the polymerization proceeded through the reaction at the anomeric position. The ^{13}C NMR spectrum of the product in D_2O showed peaks at δ 39.3 - 46.7 due to C1 and C6, peaks at δ 67.3 - 76.3 due to C3 - C5, and peaks at δ 92.8 and 96.7 due to C2. No observation of the peak due to a carbonyl carbon supported the ring structure of the product polymer. If glycosylamine structure exists, the peak corresponding to C1 of *N*-glycoside generally appears at around δ 85. No such peak was observed at that region in the ^{13}C NMR spectrum of the product polymer. Although the peak at δ 161.2 ascribable to Schiff base (C=N) appeared, the content of the Schiff base structure in the product polymer may be low, if any. Because the absorption at around 1650 cm^{-1} due to C=N in the IR spectrum of the product polymer was very small. The all above spectroscopic data support that the polymerization of **1a** proceeded via Amadori rearrangement to give aminopolysaccharide **2** mainly having aminoketose structure.



Scheme 2.

Table 1. Polymerization of 6-amino-6-deoxy-D-glucose (**1a**) in the presence of acetic acid[a]

	Polymerization		Acetylation		
Entry	Time /h	Yield /%[b]	Yield /%[c]	Mn[d]	Mw/Mn[d]
1	2.0	69.0	56.3	9100	1.4
2	3.0	70.2	66.4	13000	1.3
3	3.5	56.7	59.1	11000	1.3
4	4.0	45.7	53.7	9400	1.3

[a]The polymerization was carried out as described in the text. [b]Ethanol insoluble part. [c]Diethyl ether insoluble part. [d]Determined by GPC with DMF eluent.

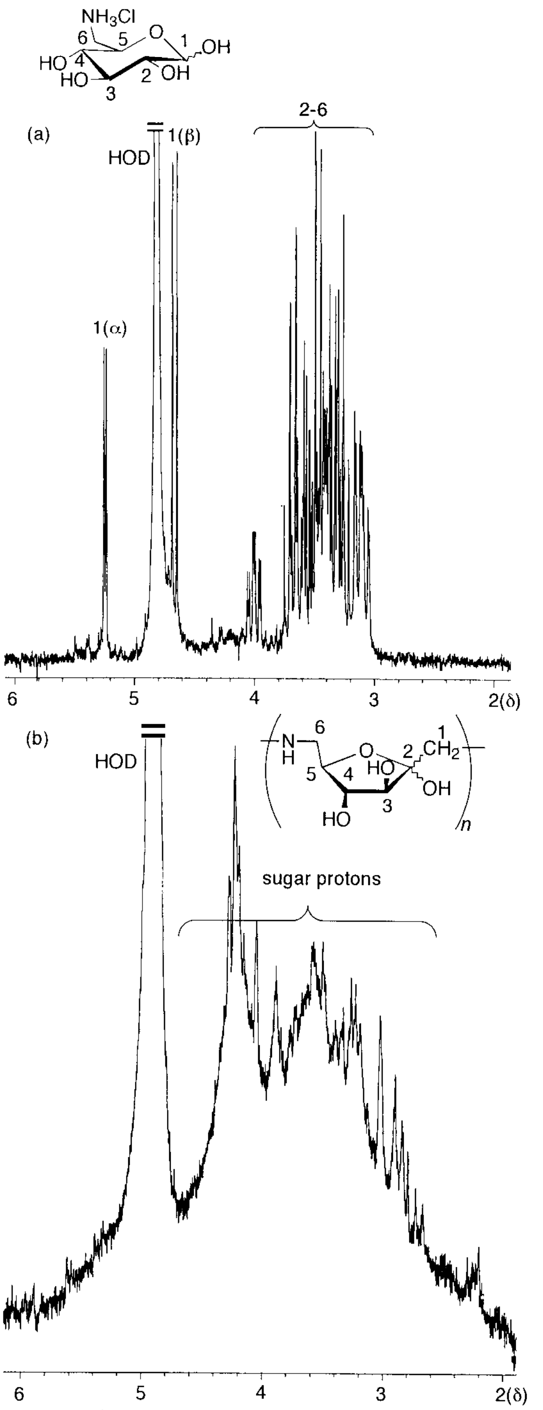
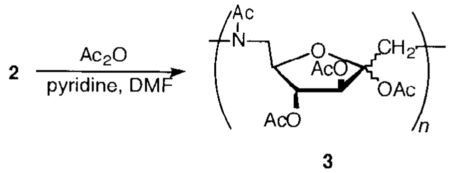


Figure 1. ^{1}H NMR Spectra of **1a** (a) and **2** (b) in D_2O.

To estimate the molecular weight of **2** by gel permeation chromatographic (GPC) measurement, acetylation of **2** was carried out in acetic anhydride / pyridine / DMF system (Scheme 3). The structure **3** of the acetylated polymer was confirmed by ^{1}H NMR and IR analyses[7] and its molecular weight was estimated by GPC with DMF eluent with a calibration curve of polystyrene standards.



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Scheme 3.

Table 1 summarized the polymerization results of **1a**. The highest yield and molecular weight were 70.2 % and 13000, respectively, given by the reaction time of 3 h. The longer reaction time than 3 h, however, gave lower yield and molecular weight, probably because of the occurrence of degradation of polymer during the reaction.

In conclusion, thermal polymerization of monomer **1a** in the presence of acetic acid gave aminopolysaccharide **2** having aminoketose structure. This is the new method for the synthesis of aminopolysaccharide. More detailed study is now in progress.

References and Notes

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7 ^{1}H NMR (DMSO-d_6 or acetic acid-d_4) δ 2.04 (br s, 12H, CH_3), 3.00 - 5.65 (br, 7H, sugar protons); IR (KBr) 1735 cm^{-1} (C=O of ester), 1637 cm^{-1} (C=O of amido).