

HYDROTHERMOLYSIS OF THE FULLY BENZYLATED α -CYCLODEXTRIN

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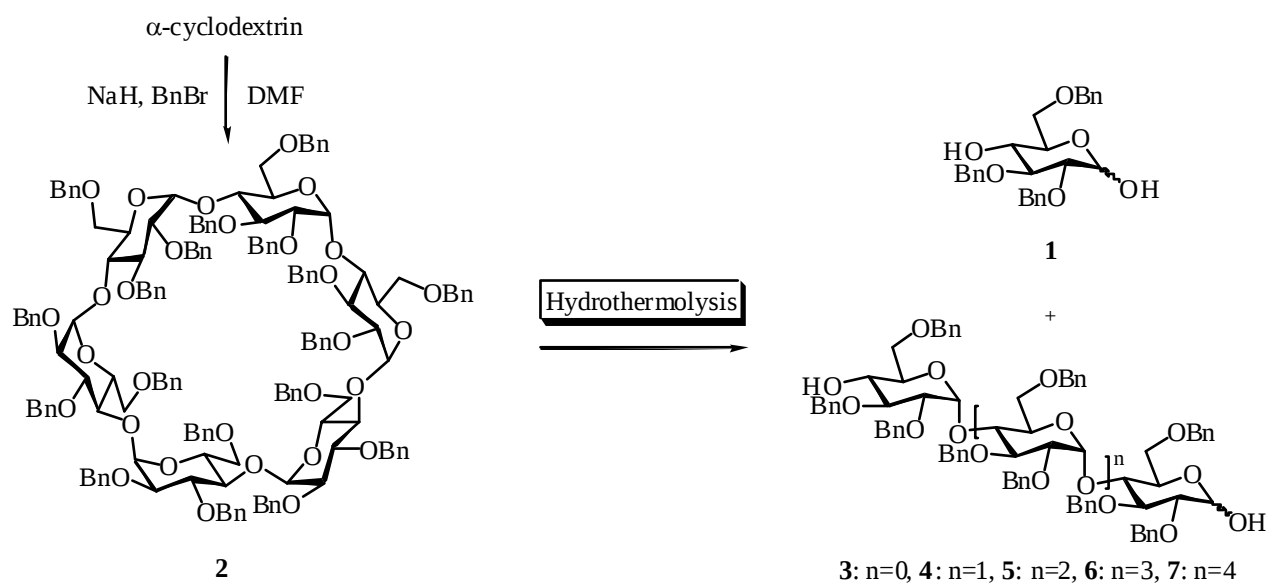
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Abstract—The treatment of the fully benzylated α -cyclodextrin with the hot compressed mixed solvent of dioxane/water (v/v=1/1) at 270 °C and 150 kg/cm² for 40 min afforded 2,3,6-tri-*O*-benzyl-D-glucopyranose in good yield. The hydrothermolysis of the fully benzylated α -cyclodextrin at 240 °C produced partially benzylated maltooligosaccharide derivatives.

Hydrothermal reactions are becoming significant for developing the utilization technology of polymeric biomass resources.¹ Hydrothermal cleavage of glycosidic bonds is characterized by the addition of only water,¹ and the saccharification processes of converting cellulose to glucose by hydrothermal treatment without a catalyst are now being widely investigated.¹⁻⁴ Some sugar moieties are often obtained from naturally existing oligosaccharides by acid hydrolysis and/or enzymatic hydrolysis.^{5,6} Recent studies showed that protected cyclodextrins were suitable substrates to prepare protected glucose and maltooligosaccharide derivatives which are important compounds in synthetic carbohydrate chemistry. The acetolytic cleavage of a single glycosidic bond of the fully acylated cyclodextrins gave the fully acylated maltooligosaccharide derivatives,^{7,8} which are useful precursors for the synthesis of some artificial cyclooligosaccharides.^{9,10} The acidic hydrolysis of all the glycosidic bonds of the fully benzylated α -cyclodextrin (**2**) afforded 2,3,6-tri-*O*-benzyl-D-glucopyranose (**1**),¹¹ which is useful as a glycosyl intermediate. However, it seemed that, judging from the reported yield of **1**, the steric hindrance of the benzyl groups of **2** made the hydrolysis of the glycosidic bonds of **2** difficult even under the severe acidic conditions using 75% H₂SO₄-1,4-dioxane at 100 °C.

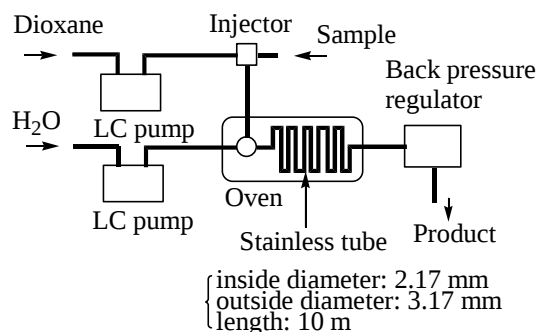
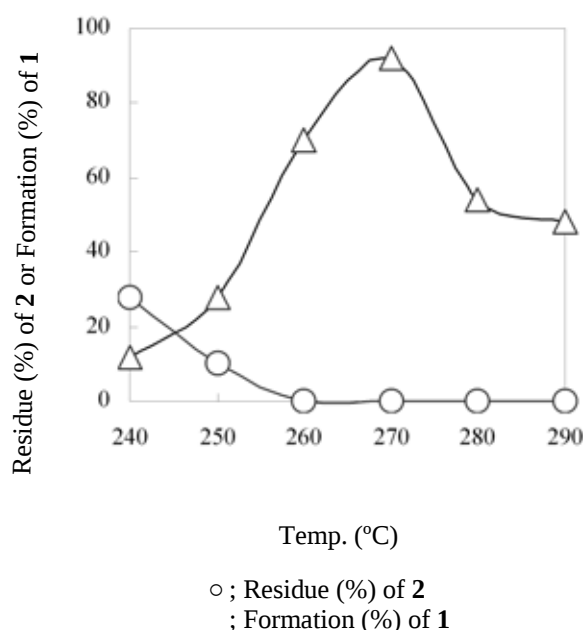
In this paper, we demonstrated the synthesis of **1** and partially benzylated maltooligosaccharide derivatives (**3-7**) by the hydrothermolysis of the glycosidic bonds of **2** in order to reveal not only the ability of the hydrothermal reaction to cleave the glycosidic bonds of the benzylated oligosaccharides but also the stability of the benzyl group toward hydrothermal treatment (Scheme 1).¹²

The benzylated α -cyclodextrin (**2**) was prepared using sodium hydride and benzyl bromide in DMF



Scheme 1. The hydrothermolysis of fully benzylated α -cyclodextrin (**2**).

according to the literature.¹³ In order to dissolve **2**, dioxane was used as the solvent combined water. Compound (**2**) dissolved in dioxane was inserted to the dioxane line from the injector and water was pumped through another line to provide the volume ratio of dioxane/water=1/1 (Scheme 2). We investigated in detail several reaction temperatures under the constant pressure of 150 kg/cm² for 40 min. The hydrothermolized mixtures were analyzed by HPLC.¹⁴ The decreased rate of **2** and the hydrolyzed yield to **1** in the range from 240 to 290 °C are shown in Figure 1. At 240 °C, HPLC analysis suggested that the production of **1** was slightly observed and several maltooligosaccharide derivatives were produced by the partial hydrolysis of **2**. The production of **1** increased with an increase in temperature. Compound (**2**) disappeared at 270 °C, and **1** was obtained in the maximum yields of 94% from **2**. For the reaction



Scheme 2. Equipment for hydrothermal reaction.

Figure 1. Hydrothermolysis of **2** and production of **1**.

conditions over 270 °C, the decomposition of **1** was observed and the yield of **1** decreased. Moreover, the isolation of **1** was attempted. The hydrolyzed products obtained by the reaction at 270 °C and 150 kg/cm² for 40 min were purified by preparative TLC to give **1** in 79% yield from **2**.¹⁵

Next, we examined the isolations of the partially benzylated maltooligosaccharides produced in the hydrothermal reaction at 240 °C for 70 min. HPLC analysis of this reaction indicated main six peaks including one of **1**. The products of the six peaks were separated by preparative TLC. The yields and molecular mass values by ESI-TOF mass spectrometry of the isolated products are summarized in Table 1. The found mass values were in fair agreement with the calculated mass values of benzylated maltooligosaccharides (**3-7**). The total isolation yields of **1-7** reached about 80%.

Table 1. Products by hydrothermolysis of benzylated α -cyclodextrin (**2**) at 240 °C for 70 min.

Compound	Yield (%)	ESI-MS m/z [M+Na] ⁺	
		Found	Calcd
1	18.3	473.1894	473.1940 for C ₂₇ H ₃₀ O ₆ Na
3	6.6	905.3573	905.3877 for C ₅₄ H ₅₈ O ₁₁ Na
4	8.8	1337.5330	1337.5814 for C ₈₁ H ₈₆ O ₁₆ Na
5	11.8	1769.7244	1769.7750 for C ₁₀₈ H ₁₁₄ O ₂₁ Na
6	12.3	2201.8674	2201.9687 for C ₁₃₅ H ₁₄₂ O ₂₆ Na
7	21.1	2634.1055	2634.1628 for C ₁₆₂ H ₁₇₀ O ₃₁ Na

As mentioned above, we found that the fully benzylated α -cyclodextrin was smoothly hydrothermolized to give the corresponding partially benzylated glucose derivatives in high yield at 270 °C and 150 kg/cm² for 40 min using the hot compressed mixed solvent of dioxane-water. The reaction at 240 °C for 70 min afforded all of the maltooligosaccharide derivatives having 2-6 glucose moieties by the partial hydrolysis of the fully benzylated α -cyclodextrin. These hydrothermal reactions were carried out without damaging their benzyl groups. This study showed that the hydrothermal reaction would be a useful method for preparing important compounds in synthetic carbohydrate chemistry.

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12. To the best of our knowledge, there have been no reports on the hydrothermolysis of the glycosidic bonds of α -(1-4)-linked oligosaccharides. We also investigated the hydrothermolysis from unprotected α -cyclodextrin and maltose to glucose. These results will be submitted in the near future.
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14. Reaction mixtures were analyzed on an ODS-3 column (4.6x300 mm) using CH₃CN at a flow rate of 0.8 mL/min.
15. The acetylation of the product (**1**) using acetic anhydride-pyridine quantitatively gave the diacetylated compound, and the ¹H NMR spectra of H-1 of this compound indicated the pyranose ring: ¹H NMR (CDCl₃): δ 5.63 (d, J =7.8 Hz, H-1 β), 6.34 (d, J =3.4 Hz, H-1 α).