NOTE

Regioselectively Modified Stereoregular Polysaccharides. III. Copolymerization between 1,6-Anhydro-3-O-acetyl-2,4-di-O-benzyl- and 1,6-Anhydro-2,3,4-tri-O-benzyl-β-D-glucopyranoses

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Stereoregular polysaccharides have been synthesized by cationic ring-opening polymerization of tri-O-substituted 1,6-anhydro sugars followed by the removal of the protecting groups.[1-3] Recently, other 1,6-anhydro sugar derivatives, which were substituted by two different types of protecting groups, have proved versatile precursors of regioselectively modified (1→6)-α-D-glucopyranans.[4-8] We reported that the polymerization of 1,6-anhydro-3-O-acetyl-2,4-di-O-benzyl-β-D-glucopyranose (1), followed by deacetylation, gave a regioselectively blocked polysaccharide 2,4-di-O-benzyl-(1→6)-α-D-glucopyranan.[4] This compound has a free OH group only in position 3 of its repeating pyranose unit. The hydroxylated polymer was also prepared by Ito and Schuerch[5] according to a similar procedure starting from the corresponding 3-O-crotyl monomer, 1,6-anhydro-2,4-di-O-benzyl-3-O-but-2-enyl-β-D-glucopyranose (DBCGL). It is expected that well-defined chemical transformations of the hydroxyl group will lead to new types of modified (1→6)-α-D-glucopyranans which are a model system of natural dextrans for the investigation in the fields of allergy, enzymology, and immunology.[1,2,5]

The physiological and pharmaceutical activities of natural polysaccharides are sometimes affected significantly by a slight structural change. Therefore, the introduction of well characterized foreign structures is an important method for obtaining information regarding the relations between properties and structures.[5,9,10] One conventional procedure often employed for this purpose is the copolymerization of appropriate monomers.[5,11-17] From this point of view, we carried out the copolymerization between 1 and 1,6-anhydro-2,3,4-tri-O-benzyl-β-D-glucopyranose (2) and compared the system with that between DBCGL and 2.

1   2

Ac, COCH$_3$;   Bn, CH$_2$C$_6$H$_5$
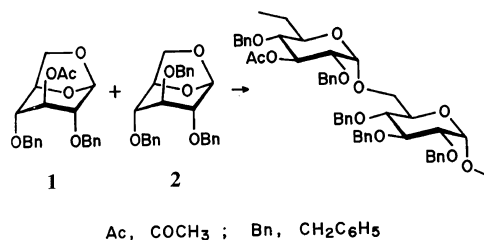
EXPERIMENTAL

1,6-Anhydro-3-O-acetyl-2,4-di-O-benzyl-β-D-glucopyranose (1) and 1,6-anhydro-2,3,4-tri-O-benzyl-β-D-glucopyranose (2) were synthesized and purified according to methods previously described.[4,18] Dichloromethane and p-chlorobenzenediazonium hexafluorophosphate were purified in the usual manner. Copolymerization was carried out using high-vacuum polymerization techniques.[4,18]

^{1}H and ^{13}C NMR spectra were recorded with

Table I. Copolymerization of 1,6-anhydro-3-O-acetyl-2,4-di-O-benzyl-β-D-glucopyranose (1) with 1,6-anhydro-2,3,4-tri-O-benzyl-β-D-glucopyranose (2) at −60°C[a]

Exptl. No.	Feed 1 g	Feed 2 g	Mole fraction of 1 in feed	Initiator mol% to monomer	Polymerization time min	Yield %	Mole fraction of 1 in copolymer[b]	$[\eta]$[c]	$[\alpha]_D^{25}$ deg
3	0	1.728	0	5	12	85.0	—	0.78	112.0
8	0.155	1.555	0.10	5	7	29.9	0.06	0.47	112.5
9	0.310	1.384	0.20	5	10	27.3	0.06	0.41	114.5
10	0.462	1.192	0.30	5	14	20.4	0.15	0.27	118.2
11	0.616	1.040	0.40	5	19	8.5	0.17	0.20	119.4
12	0.770	0.847	0.51	5	23	9.8	0.19	0.13	117.4
13	0.921	0.692	0.60	10	50	25.3	0.28	0.17	119.8
14	1.074	0.517	0.70	10	120	23.6	0.33	0.14	120.1
15	1.229	0.346	0.80	10	210	15.7	0.45	0.09	122.8
16	1.381	0.175	0.90	10	240	13.5	0.58	0.13	122.9
17	1.538	0	1.0	10	3720	23.5	—	0.10	130.0

[a] Total monomers, 4×10^{-3} mol; initiator, phosphorus pentafluoride; solvent, dichloromethane, 4 ml.
[b] Determined by ^{1}H NMR spectroscopy.
[c] Determined in chloroform at 25°C.

JEOL JNM-MH-100 NMR and JEOL JNM-FX-100 Fourier transform NMR spectrometers, respectively. CDCl$_3$ was used as the solvent and tetramethylsilane as an internal reference. Optical rotations were determined in a JASCO DIP-4 automatic polarimeter with a 1-dm cell. Intrinsic viscosities were measured in a Ubbelohde viscometer at 25°C. TLC was carried out on Merck silica gel 60 F$_{254}$ coated plates with use of a benzene–ether (9 : 2 v/v) mixture as solvent.

RESULTS AND DISCUSSION

Copolymerization between **1** and **2** was carried out under high vacuum at $-60°C$ with PF$_5$ catalyst in anhydrous dichloromethane (Table I). High catalyst concentrations of 10 and 5 mol% PF$_5$ were used. Copolymerization was terminated at 10—30% conversion by judging the mobility of the polymerization solution. A white powdery solid was obtained.

The TLC retention value (R_F) of the copolymerization product was intermediate between those of each homopolymer: 0.55 for the polymer No. 16, 0.11 for the homopolymer of **1**, and 0.88 for the homopolymer of **2**. It was determined definitely that the polymer was not a mixture of each homopolymer, although none of the extra signals due to the alternating diad fraction could be detected in any of the IR, CD, ^{1}H-, and ^{13}C NMR spectra. There appeared no β-anomeric resonance in the ^{13}C NMR spectra, suggesting that the copolymer were highly streoregular.

Mole fraction of the 3-O-acetyl-2,4-di-O-benzyl-(1→6)-α-D-glucopyranosyl unit in copolymer was determined from the area ratio of acetyl/aromatic ^{1}H NMR signals. As shown in Table I, the amount of the **1** unit incorporated into the copolymer was less than that in the feed. The intrinsic viscosities of the copolymers decreased with an increase in the composition of **1**. Apparently, monomer **1** was less reactive than **2**. It was also found that specific rotations of the copolymers were related linearly to the weight fraction of **1** in copolymer.

Approximate instantaneous reactivity ratios were evaluated by the Kelen–Tüdos method,[19] the applicability of which indicated clues to the copolymerization mechanism.[2,15–17,19–21] The data from experiments 8 and 10 deviated from the plots of the other data and were excluded in the final evalua-
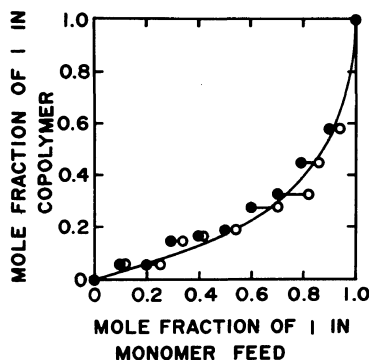

Figure 1. Composition curve for the copolymerization of 1,6-anhydro-3-O-acetyl-2,4-di-O-benzyl-β-D-glucopyranose (**1**) with 1,6-anhydro-2,3,4-tri-O-benzyl-β-D-glucopyranose (**2**). ●, initial monomer composition; ○, final monomer composition; curve, calculated from the reactivity ratios $r_1 = 0.06$ and $r_2 = 3.3$.

tion of the reactivity ratios ($r_1 = 0.10$, $r_2 = 3.3$) since these copolymers contained a small amount of acetyl group and were sensitive to experimental error. The integrated copolymer composition equation of Mayo and Lewis[22] gave the reactivity ratios of $r_1 = 0.06 \pm 0.05$ and $r_2 = 3.3 \pm 1.0$. The instantaneous copolymer composition curve calculated from the reactivity ratios is shown in Figure 1. The position of the horizontal lines represents the copolymer composition and the length of the horizontal lines corresponds to the range of the monomer composition from the feed to the final solution.[11–13,15,16]

This copolymerization system can be compared with that of the 3-O-crotylated monomer DBCGL and **2**.[5] The monomer reactivities of 1,6-anhydro-β-D-glucopyranose derivatives are in the order of DBCGL > **2** > **1**. The low monomer reactivity of **1** may be ascribed primarily to the basic carbonyl group. The carbonyl oxygen was capable of interfering with the nucleophilic approach of the acetal oxygen to the propagating center. It is also reasonable to assume that the propagating oxonium ion of the terminal **1** unit can be stabilized by solvation of the neighboring carbonyl group. In addition, the basicity of the carbonyl group also contributes to the slow initiation: the catalyst efficiency can be decreased by a complex formation of the acetyl group with the Lewis acid catalyst.[4]

Compared with the DBCGL–**2** combination, the

low molecular weight of the copolymers may be a demerit of the present system. However, it seems that this demerit could be cancelled to some extent by the ease of deacetylation. The degree of polymerization scarcely decreased during the deacetylation, which proceeded completely under mild conditions in high yield.[4] This is in contrast with the reported significant decrease in DP during the decrotylation.[5]

Thus, the copolymers prepared from **1** and **2** may find possible application in the synthesis of modified stereoregular $(1\rightarrow6)$-α-D-glucopyranans. The composition and sequence distributions different from those of the DBCGL–**2** copolymers may serve to elucidate certain structural problems.

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