Ring-Opening Polymerization of 3-*O*-Benzyl-*β*-L-arabinofuranose 1,2,5-Orthopivalate and Synthesis of Stereoregular (1→5)-α-L-Arabinofuranan

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ABSTRACT: The ring-opening polymerization of 3-*O*-benzyl-*β*-L-arabinofuranose 1,2,5-orthopivalate (**1**) by BF_3·Et_2O gave stereoregular 3-*O*-benzyl-2-*O*-pivaloyl-(1→5)-α-L-arabinofuranan with $[\alpha]_D^{25}$ −151.4° and a number-average degree of polymerization ($\overline{DPn}$) of approximately 91. These results indicate that the substituted effects derived from the chemical synthesis of cellulose by ring-opening polymerization can be also applied to that of the arabinose ortho ester derivative. Removal of the pivaloyl and benzyl groups gave a linear stereoregular polysaccharide (1→5)-α-L-arabinofuranan.

Introduction

Arabinans, mainly composed of α-L-arabinofuranosyl residues, are generally arranged in (1→5)-linked chains with varying numbers of residues substituted with other α-L-arabinofuranosides at the C2- and/or C3-position. Although a linear (1→5)-linked α-L-arabinofuranan has been reported in processed apple juice[1] and from the seeds of guapuruvu (*Schizolobium parahybum*),[2] much remains unknown about the relationship between their structure and properties. Thus, we need the chemical syntheses of polymers with definite structures.

Kochetkov et al. reported the polymerization of the tricyclic orthobenzoate of arabinofuranose:[3] that is, the polymerization of 3-*O*-acetyl-*β*-L-arabinofuranose 1,2,5-orthobenzoate was run in nitromethane with catalytic amounts of mercuric bromide in the presence of small amounts of 1,2,3,4-tetra-*O*-acetyl-*β*-D-glucopyranose, which served as the reaction initiator with the hydroxyl group. The polymer was a linear α-glycosidically linked arabinofuranan with a $\overline{DPn}$ up to 60, but consisting of a mixture of at least 90% of (1→5)-arabinofuranosidic linkage and about 8−10% of (1→2)-arabinofuranosidic linkage. Thus, stereoregular (1→5)-α-arabinofuranan has not synthesized yet from arabinose 1,2,5-ortho ester derivatives.

Backnowsky et al. have reported that the polycondensation of 3-*O*-benzoyl-1,2-cyanoethylidene-5-*O*-trityl-*β*-L-arabinofuranoside gave stereoregular (1→5)-α-L-arabinofuranan with $\overline{DPn}$ = 15−23.[4] However, it would not be suitable for the investigation of the relationships between structures and functions depending on the substituents at C2- and C3-positions, because the synthesized polymer has the same protective groups at both C2- and C3-positions.

Uryu et al. described that stereoregular (1→5)-α-L-arabinofuranan derivative was obtained by the ring-opening polymerization of 1,4-anhydro-2,3-di-*O*-*tert*-butyldimethylsilyl-α-L-arabinopyranose.[5] However, they could not get pure (1→5)-α-L-arabinofuranan after the deprotection.

We have performed the ring-opening polymerizations of a variety of sugar ortho ester derivatives and found that substituents on the monomer played an important role in stereo- and regioregularity of the resulting polymer;[6−9] i.e., both 3-*O*-benzyl and 2-*O*-pivaloyl groups are indispensable for the stereoregular ring-opening polymerization. On the basis of this knowledge, we expect that the ring-opening polymerization of 3-*O*-benzyl-*β*-L-arabinofuranose 1,2,5-orthopivalate (**1**), different from that of 3-*O*-acetyl-*β*-L-arabinofuranose 1,2,5-orthobenzoate tried by Kochetkov et al.,[3] leads to a linear stereoregular 3-*O*-benzyl-2-*O*-pivaloyl-(1→5)-α-L-arabinofuranan. This (1→5)-α-L-arabinofuranan derivative has a good possibility of synthesizing regiospecifically branched arabinofuranan, owing to the ready distinction between C2- and C3-positions. Moreover, the ring-opening polymerization may give the polymer with higher molecular weight than that of the polymer by the polycondensation by Backnowsky et al.,[4] because the enhancement of polymerizability by the 3-*O*-benzyl group is expected from our earlier results.[6−9]

In the present paper, we report the synthesis of a linear stereoregular (1→5)-α-L-arabinofuranan by the ring-opening polymerization of 1,2,5-orthopivalate (**1**).

Table 1. Polymerization of 3-*O*-benzyl-*β*-L-arabinofuranose 1,2,5-orthopivalate[a]

entry	initiator	temp (°C)	time (h)	yield (%)	$[\alpha]_D^{25}$ (deg)	$\overline{DPn}$[b]	M_w/M_n
1	Ph_3CBF_4	20	42	94	−125.4	17.2	1.46
2	Ph_3CBF_4	0	123	98	−133.8	17.6	1.12
3	Ph_3CBF_4	−80	237	55	−147.7	19.7	1.14
4	$SbCl_5$	−30	139	69	−137.5	34.0	1.39
5	$SbCl_5$	−80	238	56	−124.8	17.8	1.10
6	PF_5	−30	48	89	−114.9	31.3	1.48
7	BF_3·Et_2O	0	52	97	−142.4	50.5	1.97
8	BF_3·Et_2O	−30	137	95	−151.4	90.6	1.48
9	BF_3·Et_2O	−80	237	71	−159.2	16.1	1.09

[a] Initiator concentration: 5 mol %; solvent: CH_2Cl_2; monomer/solvent: 70 g/100 mL. [b] Molecular weight was calculated from GPC data using polystyrene standard.

Results and Discussion

Polymerization of the Ortho Ester 1. The synthesis of compound **1** has been reported in our previous paper.[10] The reaction conditions and results of the ring-opening polymerizations are summarized in Table 1. All polymerizations were carried out at the same initiator

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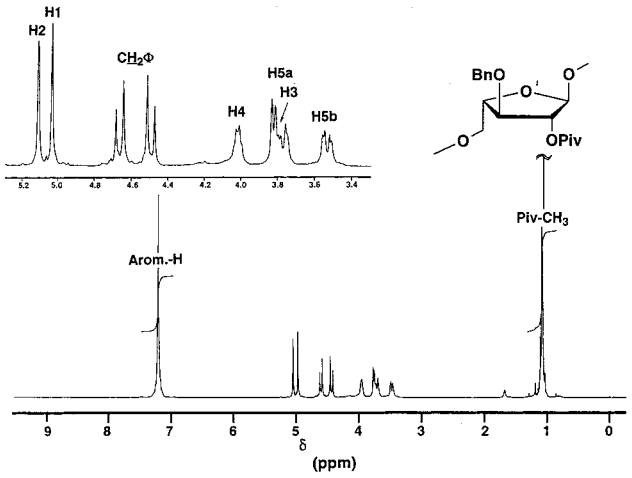


Figure 1. The 300 MHz ^{1}H NMR spectrum of 3-*O*-benzyl-2-*O*-pivaloyl-(1→5)-α-L-arabinofuranan ($CDCl_3$ as solvent).

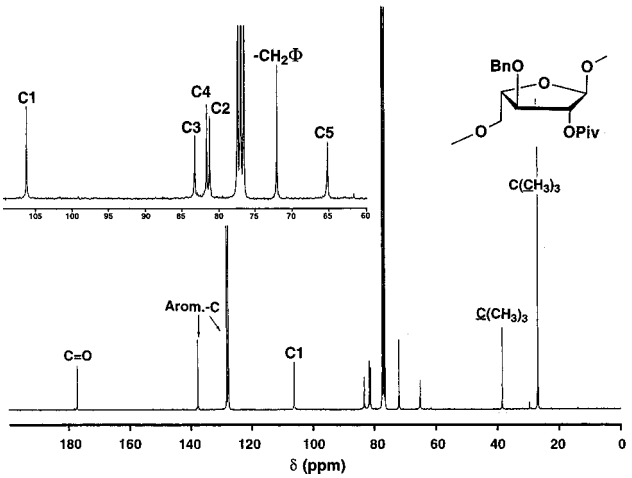


Figure 2. The 300 MHz ^{13}C NMR spectrum of 3-*O*-benzyl-2-*O*-pivaloyl-(1→5)-α-L-arabinofuranan ($CDCl_3$ as solvent).

(5 mol %) and monomer (70 g/100 mL) concentrations in dichloromethane. The highest DPn, approximately 91, was obtained in the polymerization at −30 °C using BF_3·Et_2O as an initiator.

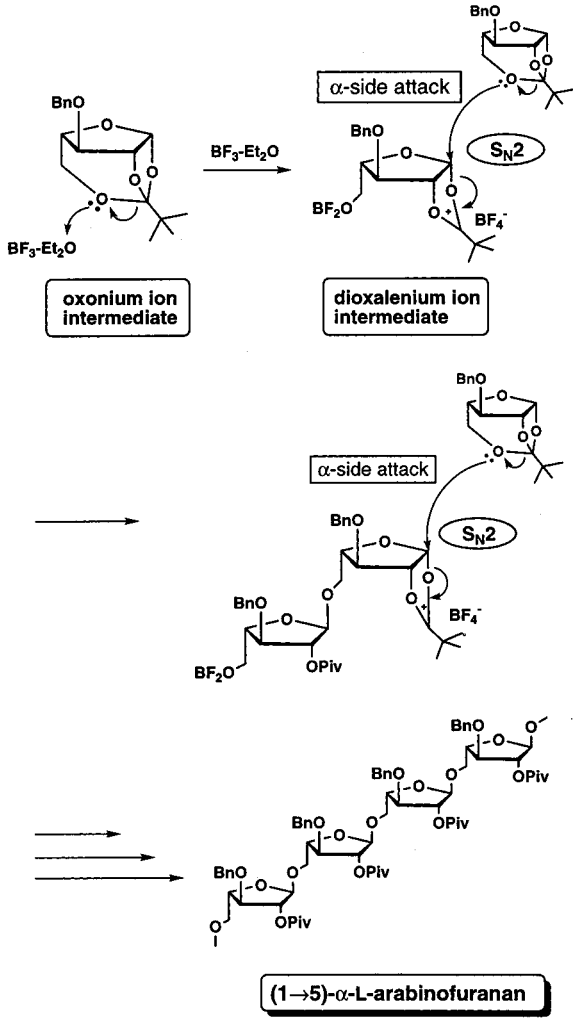
Structure of Polymers. In general, there are four possible structural units in the polymer prepared by the ring-opening polymerization of 3-*O*-benzyl-*β*-L-arabinofuranose 1,2,5-orthopivalate, namely, (1→5)-α-, (1→5)-*β*-, (1→2)-α-, and (1→2)-*β*-arabinofuranosidic units.

As shown in Table 1, all resulting polymers had very large negative specific rotations from −115° to −159°. This suggests that these polymers have α-arabinofuranosidic linkages: only α-L-arabinofuranoside has been reported to have large negative specific rotation in four kinds of methyl L-arabinosides, i.e., α-, *β*-furanosides and α-, *β*-pyranosides.[11]

The ^{1}H and ^{13}C NMR spectra of the polymer entry 8 shown in Table 1 are shown in Figures 1 and 2, respectively.

Figure 1 shows very clear resonance for each ring proton; especially the signal of anomeric proton appears at *δ* 5.03 ppm as a singlet. This clearly indicates that the polymer has highly stereoregularity and consists of only α-furanosidic linkages, because the corresponding anomeric proton of *β*-arabinofuranosidic unit is expected to appear as a doublet (J = approximately 4.2−4.5 Hz) from the data reported so far.[12] The signal of the C2

Scheme 1. Mechanism of the Ring-Opening Polymerization of Compound 1



proton appears in the lowest magnetic field, i.e., *δ* 5.11 ppm, in the furanosidic ring protons. This supports that the polymer has the pivaloyl group at the 2-*O*-position, not at the 5-*O*-position, indicating that the polymer has surely (1→5)-furanosidic linkages. The ^{13}C NMR spectrum also shows a sharp singlet peak for anomeric carbon at 106.2 ppm and also very clear resonances for other ring carbons, indicating that the polymer has high regio- and stereoregularity.

Thus, these results strongly indicate that the synthesized polymer was exactly stereoregular (1→5)-α-L-arabinofuranan as expected. Scheme 1 illustrates the proposed propagation mechanism of the polymerization of compound **1** to yield stereoregular (1→5)-α-L-arabinofuranan.

The ^{1}H and ^{13}C NMR spectral patterns of the polymer entry 7 were completely identical with those of entry 8. However, the polymer entries 1−6 and 9 were mixtures consisting of over 90% (1→5)-α-furanosidic unit. These results reveal that the attack of an initiator on a C2 or C5 oxygen in compound **1** leading to (1→2)- or (1→5)-α-furanosidic unit is largely affected by the initiators used and also reaction temperatures.

Conversion into (1→5)-α-L-Arabinofuranan. Both debenzylation and deacylation of 3-*O*-benzyl-2-*O*-pivaloyl-(1→5)-α-L-arabinofuranan were conducted with sodium metal in liquid ammonia and anhydrous tetrahydrofuran as a cosolvent at −50 °C, resulting in

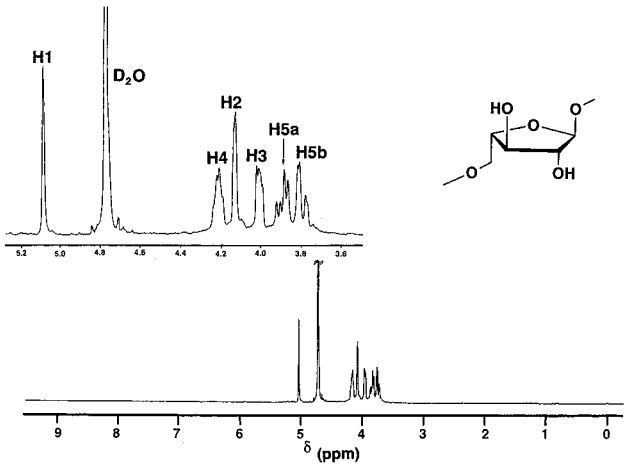


Figure 3. The 300 MHz ^{1}H NMR spectrum of (1→5)-α-L-arabinofuranan (D_2O as solvent).

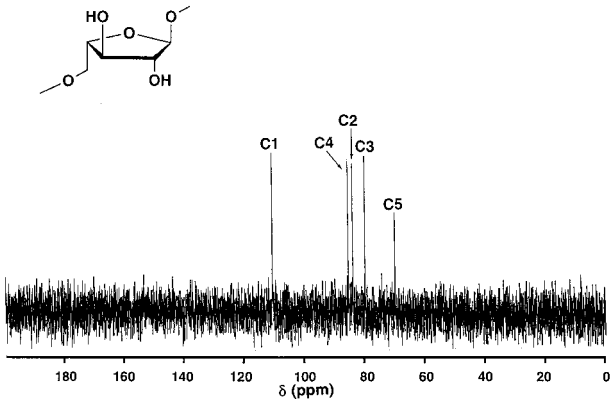


Figure 4. The 300 MHz ^{13}C NMR spectrum of (1→5)-α-L-arabinofuranan (D_2O as solvent).

(1→5)-α-L-arabinofuranan. The GPC analysis of the polymer measured in 1/15 N phosphate buffer (pH 6.90) as poly(ethylene oxide) standards indicated that the deprotections were performed without any depolymerization. The ^{1}H NMR spectrum of (1→5)-α-L-arabinofuranan in D_2O suggests that the benzyl and pivaloyl groups were completely removed (Figure 3). These ^{1}H resonances were assigned via their cross-peaks in the COSY spectrum.

Figure 4 showed the only five peaks although the $\overline{DP}n$ of the polymer is 91. The ^{13}C resonances were assigned via the cross-peaks in the CH-HETCOR spectrum. The anomeric carbon peak appears at 110.4 ppm in D_2O with sodium 3-(trimethylsilyl)propionate-2,2,3,3-d_4 as internal standard. Backnowsky et al. reported that the ^{13}C chemical shifts of their synthesized arabinofuranan [C-1, δ 108.8; C-2, δ 82.1; C-3, δ 78.1; C-4, δ 83.5; C-5, δ 68.2] measured in D_2O with methanol as internal standard at 60 °C.[4] Furthermore, Swamy et al. reported that the ^{13}C chemical shifts of natural (1→5)-α-arabinofuranan [C-1, δ 108.3; C-2, δ 81.6; C-3, δ 77.5; C-4, δ 83.1; C-5, δ 67.7] measured in D_2O with TMS as internal standard.[13] The ^{13}C chemical shifts of our synthesized arabinofuranan are almost identical with them, although a small difference (~1.6−2.1 ppm) may arise from different internal standards and temperatures.

Table 2 shows the ^{13}C chemical shifts measured in $(CD_3)_2SO$ of a natural (1→5)-linked α-L-arabinofuranan from the seeds of guapuruvu[2] and our synthesized arabinofuranan. They are almost identical.

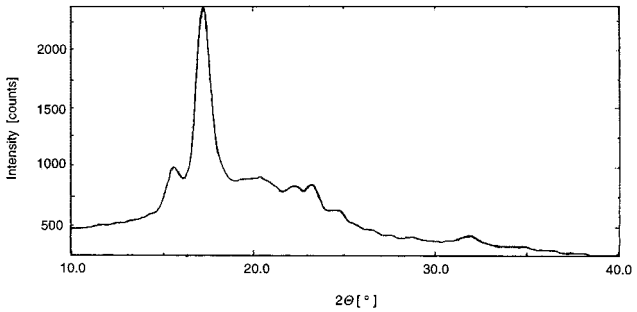


Figure 5. X-ray diffractograms of synthesized arabinofuranan.

Table 2. ^{13}C NMR Chemical Shifts Measured in $(CD_3)_2SO$ of Linear (1→5)-Linked α-L-Arabinofuranan from the Seeds of Guapuruvu and Synthesized Arabinofuranan

	chemical shifts in ppm				
compound	C-1	C-2	C-3	C-4	C-5
linear (1→5)-linked α-L-arabinofuranan from the seeds of guapuruvu	107.9	81.5	77.4	81.7	67.0
synthesized arabinofuranan	108.1	81.5	77.3	81.8	67.2

Figure 5 shows the X-ray diffractogram of the present synthesized (1→5)-α-L-arabinofuranan. The very strong intensity of $2\theta = 17.2°$ in the diffractogram is very similar to the data formerly published by Chums et al.[14]

Conclusions

The stereoregular polysaccharide (1→5)-α-L-arabinofuranan was synthesized by the ring-opening polymerization of 3-*O*-benzyl-*β*-L-arabinofuranose 1,2,5-orthopivalate. Consequently, it is demonstrated that both 3-*O*-benzyl and 2-*O*-pivaloyl groups effectively act for leading stereo- and regioregularities in the arabinofuranan synthesis, just as that of cellulose[6] and galactan.[9] Furthermore, the present synthetic method gave (1→5)-α-L-arabinofuranan with $\overline{DP}n = 91$ much higher than that of arabinan synthesized by Backnowsky et al.:[4] the enhancement of the polymerizability due to 3-*O*-benzyl group was revealed.

The present arabinofuranan derivative would be useful for the preparation of various substituted arabinans with a definite structure, which may be very useful for clarifying the relationships between structures and properties.

Experimental Section

Polymerization of Compound 1. All polymerizations were carried out under a high-vacuum system.[15] Compound **1** was dried in a polymerization ampule by evacuating for approximately a day. Methylene chloride was distilled from CaH_2 and degassed by freezing and thawing three times in a high-vacuum line. The solvent was transferred under high vacuum. Triphenylcarbenium tetrafluoroborate was placed in the reaction ampule with compound **1**. $BF_3{\cdot}Et_2O$ and $SbCl_5$ were added into the reaction ampule through a rubber septum by syringe. Phosphorus pentafluoride was generated from *p*-chlorobenzenediazonium hexafluorophosphate by decomposition at 160 °C and transferred to the reaction ampule. The reaction apparatus was then separated by melting off and placed in a bath of appropriate temperature. The reaction mixture was diluted with chloroform, washed with saturated aqueous $NaHCO_3$, water, and brine, dried over anhydrous sodium sulfate, and concentrated to dryness. The polymer mixture was dissolved in a small amount of chloroform. To the solution was added *n*-hexane, and then precipitated polymer 3-*O*-benzyl-2-*O*-pivaloyl-(1→5)-α-L-arabinofuranan was

collected by filtration and finally dried in vacuo. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.03 (s, 1H, C1−H), 5.10 (s, 1H, C2−H), 3.82 (d, 1H, $J_{3,4}$ = 5.7 Hz, C3−H), 4.02 (m, 1H, $J_{4,5a}$ = 3.9 Hz, C4−H), 3.78 (dd, 1H, J_{gem} = 11.1 Hz, C5−Ha), 3.54 (dd, 1H, $J_{4,5b}$ = 3.6 Hz, C5−Hb), 1.14 (C═OC(CH_3)$_3$), 4.66, 4.49 (d, 1H, J = 12.0 Hz, respectively, CH_2C$_6$H$_5$), 7.26 (aromatic). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 106.2 (C-1), 81.3 (C-2), 83.3 (C-3), 81.7 (C-4), 65.3 (C-5), 72.1 (*C*H$_2$C$_6$H$_5$), 27.0 (CH_3), 38.5(C═O*C*(CH_3)$_3$) 137.7 128.3, 127.8, 127.7 (aromatic), 177.2 (C═O).

Anal. Calcd for ($C_{14}H_{16}O_5$)$_{90.6}$0.8H_2O: C, 63.6; H, 6.12. Found: C, 63.4; H, 6.08.

(1→5)-α-L-Arabinofuranan. The stereoregular 3-*O*-benzyl-2-*O*-pivaloyl-(1→5)-α-L-arabinofuranan [$\overline{DP}$n = 91] (90 mg) dissolved in anhydrous tetrahydrofuran (4 mL) distilled over potassium metal/benzophenone was added dropwise to a solution of small pieces of sodium metal in 4 mL of liquid ammonia at −50 °C. The reaction was continued for 5 h followed by successive addition of ammonium chloride and several drops of water. After the reaction mixture was allowed under a stream of nitrogen gas in order to remove ammonia. Deprotected polymer was dialyzed with water and freeze-dried (34.4 mg, 85.1% yield). ^{1}H NMR (300 MHz, D_2O): δ = 4.99 (s, 1H, C1−H), 4.03 (d, 1H, $J_{2.3}$ = 3.0 Hz, C2−H), 3.90 (dd, 1H, $J_{3,4}$ = 5.1 Hz, C3−H), 4.10 (m, 1H, C4−H), 3.79 (dd, 1H, J_{gem} = 12 Hz, $J_{4,5a}$ = 6.0 Hz, C5−Ha), 3.69 (dd, 1H, $J_{4,5b}$ = 2.4 Hz, C5−Hb). ^{13}C NMR (300 MHz, D_2O): δ = 110.4 (C-1), 83.7 (C-2), 79.6 (C-3), 85.2 (C-4), 69.7 (C-5).

Anal. Calcd for ($C_5H_8O_4$)$_{90.6}$: C, 45.4; H, 6.11. Found: C, 45.4; H, 6.11.

Measurements. ^{1}H and ^{13}C NMR, HH-COSY, and CH-HETCOR spectra were recorded with a Varian INOVA300 FT-NMR (300 MHz) spectrometer, in chloroform-*d*, D_2O, or $(CD_3)_2SO$ with tetramethylsilane (TMS) and sodium 3-(trimethylsilyl)propionate-*2,2,3,3-d*$_4$, respectively, as internal standards. Chemical shifts (δ) and coupling constants (J) are given in δ values (ppm) and hertz, respectively. Optical rotations were measured at 25 °C using a JASCO Dip-1000 digital polarimeter. Molecular weight distributions of the substituted and deprotected polymers were analyzed by gel permeation chromatography (GPC) in chloroform and 1/15 N phosphate buffer (pH 6.90), respectively. Calibration curves were obtained by using polystyrene standards (Shodex) in chloroform and poly(ethylene oxide) standards (TOSOH) in phosphate buffer. A Shimadzu liquid chromatograph injector (LC-10ATvp), a Shimadzu column oven (CTO-10Avp), a Shimadzu UV−vis detector (SPD-10Avp), a Shimadzu refractive index detector (RID-10A), a Shimadzu communication bus module (CBM-10A), a Shimadzu LC workstation (CLASS-LC10), and Shodex columns (KF802, KF802.5, and KF803) were used. The flow rate was 1.0 mL/min.

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