

STUDY ON CATIONIC RING-OPENING COPOLYMERIZATION OF 1,4-ANHYDRO-2,3-DI-O- BENZYL- α -D-RIBOPYRANOSE WITH 1,4-ANHYDRO-2,3-O-ISOPROPYLIDENE- α -D- RIBOPYRANOSE

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ABSTRACT

Cationic ring-opening copolymerization of 1,4-anhydro-2,3-O-isopropylidene- α -D-ribo-pyranose (AIRP) with 1,4-anhydro-2,3-di-O-benzyl- α -D-ribofuranose (ADBR) prepared from D-ribose was studied. Copolymerization using SbCl_5 or $\text{BF}_3 \cdot \text{OEt}_2$ as catalyst at low temperature gave stereoregular ($1 \rightarrow 4$) β -D-ribofuranan (C-1 and C-4 ring cleavage see Scheme 1) or ($1 \rightarrow 5$) α -D-ribofuranan (C-1 and C-5 ring cleavage) respectively. The effects of catalysts, reaction time and temperatures on yield and stereoregularity of the obtained polymers were studied. Polymers were characterized by molecular weight, ^1H NMR, ^{13}C NMR and optical rotation.

INTRODUCTION

In the research program devising new and efficient methods of obtaining stereoregular polysaccharides, it was found that the selective ring-opening copolymerization of 1,4-anhydro-2,3-benzylidene- α -D-ribofuranose (ABRP) with 1,4-anhydro-2,3-di-O-t-butyldimethylsilyl- α -D-ribofuranose (ADSR) at 0°C in the presence of SbCl_5 catalyst gave stereoregular copolymer with complete 1,4- β -pyranose structure, even though the ring-opening homopolymerization of ADSR gave no 1,4- β -linked polymer^[1]. Similar result was obtained by copolymerization of 1,4-anhydro-2,3-di-O-benzyl- α -D-ribofuranose (ADBR) with ABRP at almost the same condition, while

the polymerization of ADBR afforded poly (1 $\rightarrow$ 5) α -D-ribofuranan derivatives with any catalyst at low temperatures^[2]. However, ADSR and 1,4-anhydro-2,3-O-isopropylidene- α -D-ribofuranose (AIRP), having similar structure with ABRP, were readily copolymerized to afford a mixed structure of (1 $\rightarrow$ 4) β -D-pyranose and (1 $\rightarrow$ 5) α -D-ribofuranose units using SbCl_5 as catalyst^[3]. The copolymer structures of anhydrosaccharide derivatives synthesized were determined by the protective group, catalyst and polymerization temperature and time.

Moreover, it was reported that pyranose-type sulfated polysaccharides such as sulfated branched (1 $\rightarrow$ 4) β -D-pyranans^[4,5], curdlan (linear (1 $\rightarrow$ 3) β -D-glucan) sulfate^[6], and lentinan (branched) (1 $\rightarrow$ 3) β -D-glucan) sulfate^[7], exhibited high anti-AIDS virus activities. Taking account of good solubility of the copolymers consisting of different substituted ribopyranosidic units and easy removal of the protective group, the stereoregular polysaccharide synthesized by ring-opening copolymerization becomes important.

In this paper, we report that poly (ADBR-co-AIRP) was prepared by copolymerization of ADBR and AIRP using SbCl_5 and $\text{BF}_3 \cdot \text{OEt}_2$ as catalysts at various temperatures. Molecular weight and structure of the obtained copolymers were characterized by GPC, ^1H and ^{13}C -NMR respectively.

EXPERIMENTAL

1. Monomer

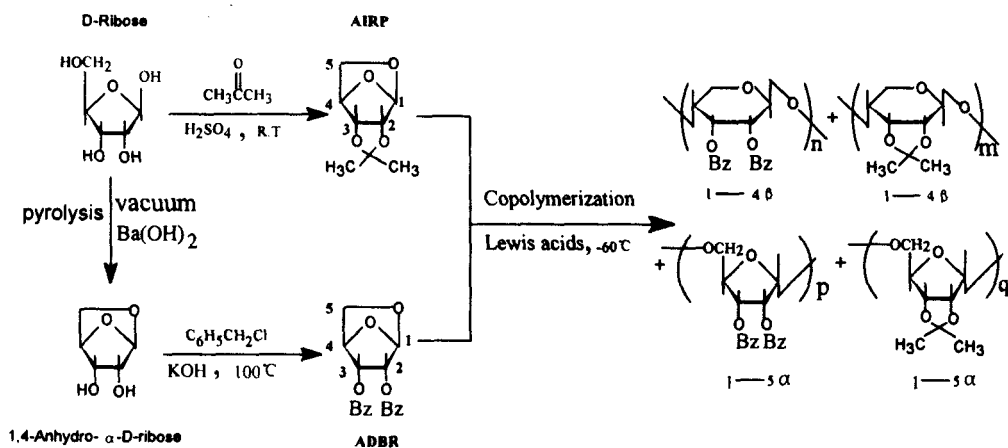
1,4-anhydro- α -D-ribofuranose was obtained by vacuum pyrolysis of D-ribose^[8]. ADBR was prepared by the reaction of 1,4-anhydro- α -D-ribofuranose with benzyl chloride^[9]. To a benzyl chloride solution (150 ml) of 1,4-anhydro- α -D-ribofuranose (25 g) was added 30 g of potassium hydroxide powder. The reaction mixture was stirred at 95°C ~ 100°C for 5 h. After evaporation, chloroform and water were added to the reaction mixture, the chloroform layer was separated. ADBR was obtained from evaporation of chloroform solution, then purified by recrystallization from ethanol three times and finally from *n*-butyl chloride. Yield, 72.1%; mp, 67°C ~ 68°C; $[\alpha]_D^{25} = -37.6^\circ$ (C 1% in CHCl_3).

AIRP was prepared according to the method of Hughes^[10]. D-ribose (36 g) was added into 720 ml acetone containing 9 ml of concentrated sulfuric acid. The mixture was stirred at room temperature for 1 h, neutralized with sodium hydroxide solution (18 g in 30 ml of H_2O) extracted with chloroform, the organic layer was washed with water, then dried in anhydrous sodium sulfate. After filtration and evaporation, the syrup was chromatographic in a column of silica, using benzene-ether (5 : 1, volume

ratio) as eluate. Recrystallization of crude crystal from n-pentane several times, pure AIRP was obtained. mp, $58.5 \sim 59.5^\circ \text{C}$; $[\alpha]_{\text{D}}^{25} = -70.2^\circ$ (C 1% in CHCl_3)

2. Copolymerization

Typical procedure for the copolymerization is as follows: A mixture of ADBR (0.27 g) and AIRP (0.17 g) was copolymerized with SbCl_5 (1.0 mole % to the monomers) as catalyst in dichloromethane (2 ml) under high vacuum at -40°C for 4 h. The polymerization was terminated by addition of methanol. The polymer solution obtained was neutralized with sodium bicarbonate solution, washed with water, dried over sodium sulfate, then concentrated to approximately 10 ml. A copolymer was purified by reprecipitation using the methanol-chloroform system three times and freeze-dried from benzene. The syntheses of monomers and their copolymerization are illustrated in Scheme 1.



Scheme 1. Synthesis and copolymerization of ADBR and AIRP

3. Measurement

The ^1H and ^{13}C NMR spectra were recorded on a JEOL GX-270 spectrometer. Specific rotation measurements were carried out on polymer solution in CHCl_3 at 25°C with a Perkin-Elmer 241 polarimeter. The molecular weight of the polymers was determined by GPC (eluate, THF) using polystyrene standards.

RESULTS AND DISCUSSION

The results of copolymerization are summarized in Table 1. In the copolymerization of ADBR and AIRP using SbCl_5 as catalyst, increasing polymerization temperature favored the formation of 1,4- β -stereoregular copolymer. When copolymerization was carried out at 0°C (Run 1-3) in various weight ratios of monomers in feeds, the copolymers with almost 1,4- β -D-ribopyranosidic structure was obtained

even it performed up to 75 mol % of ADBR in feed. Fig.1 shows the ^{13}C NMR spectra of the copolymers prepared from ADBR and AIRP (mole ratio = 1 : 1) using SbCl_5 as catalyst at 0°C , -20°C and -40°C respectively (see runs 2, 4, 6). The absorption peaks at 101.7 and 103.8 ppm (see Fig.1), were attributed to C-1 in ADBR and AIRP units with 1,5- α -furanosidic structure respectively^[11,12]. In Fig.1A, C-1 absorption peak due to 1,5- α -furanosidic structure almost disappeared. Furthermore, the absorption peaks of acetal carbons (see Fig.2C) of copoly (ADBR-AIRP) prepared at 0°C (mole ratio of AIRP/ADBR = 3 : 1), indicated that the copolymer is of (1 $\rightarrow$ 4) β -D-pyranosidic structure. The fact suggests that higher polymerization temperatures and mole ratio of AIRP/ADBR favor the formation of the 1,4- β -stereoregularity in copolymers.

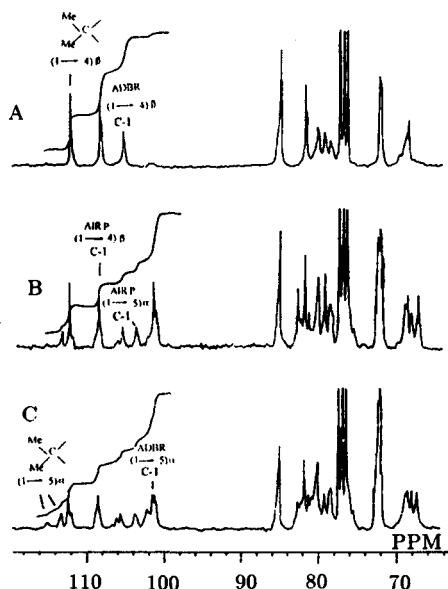


Fig.1 67.8 MHz ^{13}C NMR spectra of copoly (ADBR-AIRP) in CDCl_3 , polymerization temperature; (A) 0°C ; (B) -20°C ; (C) -40°C . Mole ratio of AIRP and ADBR: 1 : 1

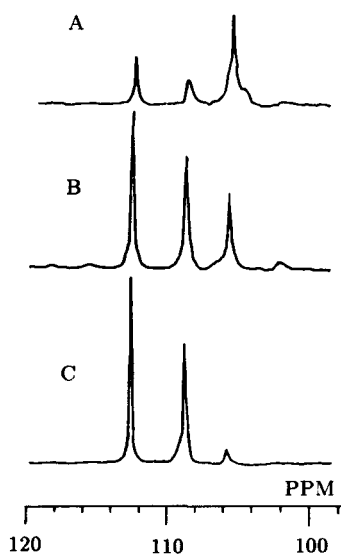


Fig.2 67.8 MHz ^{13}C NMR spectra of copoly (ADBR-AIRP) in CDCl_3 , at 0°C , SbCl_5 as catalyst. (A) AIRP:ADBR = 1 : 3; (B) AIRP:ADBR = 1 : 1; (C) AIRP:ADBR = 3 : 1

As shown in Table 1 and Fig.3, the proportion of AIRP unit in the copolymer (SbCl_5 as catalyst) prepared at 0°C was slightly higher than that in feed. However, when copolymerization at the temperature lower than -20°C (SbCl_5 or $\text{BF}_3\cdot\text{OEt}_2$ as catalyst), lower content of AIRP unit in the copolymer than that in the feed (see Table 1) demonstrates that the ring-opening polymerization of AIRP had lower reactivity than ADBP monomer did. Probably, the reason is that AIRP consisting of three rings is more stable than ADBR with two rings towards the cationic species

attacking at lower temperature. It was found that the degradation of ADBR polymer occurred along with its polymerization at 0° C^[13]. This results higher proportion of AIRP unit in the copolymer. In addition, in case of SbCl₅ as catalyst, the mole ratio of AIRP unit in the copolymer decreased as temperature decreased. For BF₃·OEt₂ as catalyst a contrast result was obtained, that is, mole fraction of AIRP unit in the copolymer increased with decreasing temperature. The reason for this phenomenon is still in study.

Table 1 Copolymerization of ADBR with AIRP

Runs	Monomer in feed			Temp.	Time	Yield	$[\alpha]_{\text{D}}^{25\text{b})}$	$\overline{M}_n$ ^{c)}	AIRP ^{d)}	Stereoregularity ^{e)} (%)			
	ADBR		AIRP							ADBR		AIRP	
	(g)	(g)	(mol%)							(°C)	(h)	(%)	(deg)
1	0.32	0.07	25	0	0.5	54.6	+15.6	0.3	24	87	13	90	10
2	0.27	0.17	50	0	0.5	54.9	-19.9	0.6	52	89	11	100	0
3	0.14	0.26	75	0	0.5	36.9	-74.3	1.0	82	100	0	100	0
4	0.27	0.18	50	-20	0.1	69.8	+42.7	1.3	44	26	74	67	33
5	0.32	0.07	25	-40	4	66.3	+81.8	1.4	18	20	80	55	45
6	0.27	0.18	50	-40	4	72.0	+74.4	1.0	41	69	31	45	55
7	0.14	0.27	75	-40	4	52.3	-3.1	1.0	68	58	42	67	33
8	0.27	0.08	33	-40	24	89.6	+105.1	3.1	20	0	100	0	100
9	0.16	0.21	67	-40	24	73.4	+50.6	2.9	56	15	85	21	79
10	0.27	0.08	33	-60	12	73.4	+101.8	2.5	32	0	100	0	100
11	0.13	0.07	67	-60	12	40.9	+53.3	1.3	61	13	87	19	81

a) Solvent: CH₂Cl₂ 2 ml; Catalyst: Run 1-7, SbCl₅, 1.0 mol%, Run 8-11, BF₃·OEt₂ 5.0 mol%

b) Measured in CHCl₃ (c 1%)

c) Determined by GPC

d) Calculated from ¹H NMR spectra

e) Calculated from ¹³C spectra

The regularity results of the copolymer suggest that the initiation step occurred from AIRP monomer, proceeded by an oxonium mechanism in the case of SbCl₅ as catalyst at a higher temperature such as 0° C. The initiating species originating from AIRP is more reactive than that from ADBR, the 1 → 4-β-linked AIRP initiating species can bind either an approaching AIRP or ADBR in such way that the 1 → 4-linked oxygen of both monomers was cleaved to give both 1 → 4-β-pyranose units. Fig.4 shows the specific rotation of the copolymer obtained at various temperatures as function of AIRP mole ratio in copolymer. The specific optical rotation of the

copolymers, a measurement of stereoregularity, depended on the polymerization temperatures, AIRP mole ratio in the copolymer and the catalysts. It decreased with the increasing temperature and the decreasing AIRP mole ratio in copolymers.

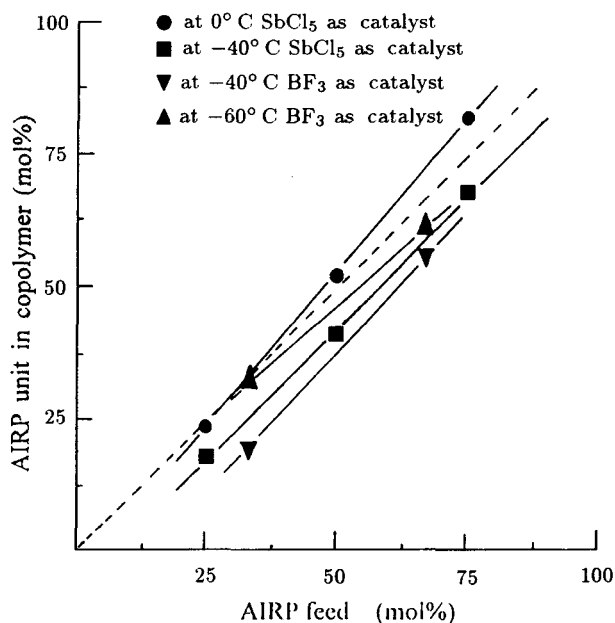


Fig.3 Variation in compositions of copoly (ADBR-AIRP) with different polymerization temperatures and catalyst

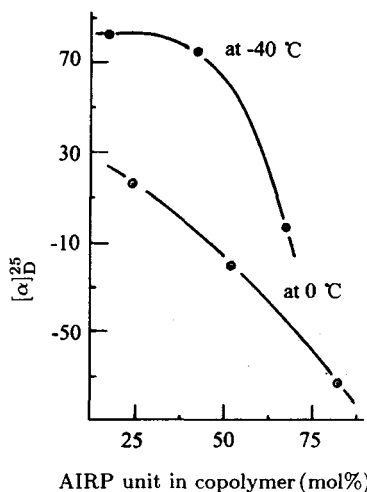


Fig.4 Specific rotation curves of copolymers obtained at different temperatures as a function of AIRP unit in copolymer (mol%), SbCl_5 as catalyst

In conclusion, it was found that ring-opening copolymerization of AIRP and ADBR with SbCl_5 as catalyst at 0°C gave a stereoregular (1 $\rightarrow$ 4)- β -linked (cellulose type) copolymer, however, complete 1,5- α stereoregular copolymer ($[\alpha]_D^{25} > 100^\circ$) was obtained when the copolymerization was carried out at lower temperatures, lower AIRP mole ratio and using $\text{BF}_3 \cdot \text{OEt}_2$ as catalyst.

Keywords:

1,4-Anhydroribose derivatives; Cationic ring-opening copolymerization; Specific rotation; Lewis acid catalysts.

REFERENCES

- [1] Yoshida, T.; Song, Li.; Wu, C.; Hatanaka, K. and Uryu, T., *Chem. Lett.*, **1991**: 477.
- [2] Hatanaka, K. and Uryu, T., *Polym. J.*, **1991**, *23*: 1383.

- [3] Wu, C.; Qiu, Y.; Pan, C.; and Uryu, T., *Functional Polym.*, **1994**, *2*: 122.
- [4] Yoshida, T.; Wu, C.; Song, L.; Uryu, T.; Kaneko, Y.; Mimura, T.; Nakashima, H. and Yamamoto, N., *Macromolecules*, **1994**, *27*: 4422.
- [5] Yoshida, T.; Katayama, Y.; Inoue, S.; and Uryu, T., *Macromolecules*, **1992**, *25*: 4051.
- [6] Yoshida, T.; Hatanaka, K.; Uryu, T.; Kaneko, Y.; Suzuki, E.; Miyano, H.; Mimura, T.; Yoshida, O. and Yamamoto, N., *Macromolecules*, **1990**, *23*: 3718.
- [7] Hatanaka, K.; Yoshida, T.; Uryu, T.; Yoshida, O.; Nakashima, H.; Yamamoto, N.; Mimura, T. and Kaneko, Y., *Jpn. J. Cancer Res.*, **1989**, *80*: 95.
- [8] Vis, E. and Fletcher, H.G. Jr., *J. Am. Chem. Soc.*, **1957**, *79*: 1182.
- [9] Zemplén, G.; Csuros, Z. and Angyal, S., *Ber. Dtsch. Chem. Ges.*, **1937**, *70*: 1848.
- [10] Hughes, N.A. and Speakman, P.R., *Carbohydr. Res.*, **1965**, *1*: 71.
- [11] Stoddart, J.F., "Stereochemistry of Carbohydrates", Wiley-Interscience, New York, **1971**: 151.
- [12] Uryu, T.; Kitano, K.; Ito, K.; Ymanouchi, J. and Matsuzaki, K., *Macromolecules*, **1981**, *14*: 1.
- [13] Uryu, T.; Ymanouchi, J.; Kato, T.; Higuchi, S. and Matsuzaki, K., *J. Am. Chem. Soc.*, **1983**, *105*: 6865.