CHEMISTRY LETTERS, pp. 477-480, 1991.

Selective Synthesis of Cellulose-Type Copolymers by Ring-Opening Copolymerization of 1,4-Anhydro-α-D-ribopyranose Derivatives

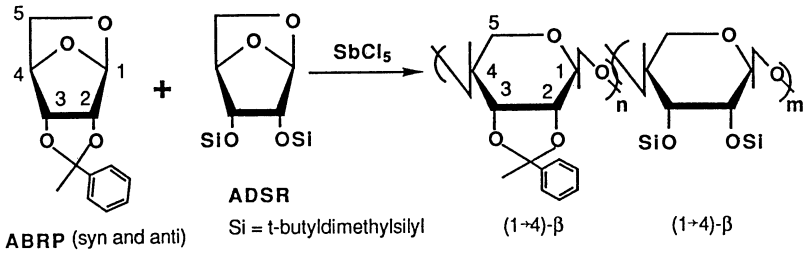
Takashi YOSHIDA, Lixin SONG, Cheng Pei WU, Kenichi HATANAKA, and Toshiyuki URYU*

Institute of Industrial Science, The University of Tokyo, Roppongi, Minato-ku, Tokyo 106

Stereoregular cellulose-type copoymers, (1→4)-β-D-ribopyranan derivatives, were prepared by selective ring-opening copolymerization of 1,4-anhydro-2,3-O-benzylidene- and -2,3-di-O-t-butyldimethylsilyl-α-D-ribopyranoses with antinomy pentachloride as catalyst at 0 °C. Being subjected to branching reaction, the copolymer can be converted into branched (1→4)-β-D-ribopyranans.

The ring-opening polymerization of anhydro sugars is one of useful methods for providing artificial stereoregular polysaccharides.[1] Previously, it was reported that the ring-opening polymerization of 1,4-anhydro-2,3-O-benzylidene-α-D-ribopyranose (ABRP) with antimony pentachloride ($SbCl_5$) as catalyst in methylene chloride at low temperature gave 2,3-O-benzylidene-(1→4)-β-D-ribopyranan in high yield, which is the first synthetic cellulose-type polysaccharide.[2] There are no reports on the synthesis of cellulose, (1→4)-β-D-glucan, by any chemical methods,[3] because it is difficult to sterically control the ring-opening mode of the corresponding 1,4-anhydro glucose monomer. 1,4-Anhydro-2,3-di-O-t-butyldimethylsilyl-α-D-ribopyranose (ADSR) was polymerized with acryloyl chloride-silver hexafluorophosphate or -silver hexafluoroantimonate complex catalyst to give (1→4)-β-D-ribopyranan derivative.[4] On the other hand, its polymerization with antimony pentachloride as catalyst afforded a polymer with a mixed structure of 1,4-β-pyranosidic and 1,5-α-furanosidic units.

Recently, it was found that such synthetic sulfated polysaccharides as curdlan (linear (1→3)-β-D-glucan) and lentinan (branched (1→3)-β-D-glucan) sulfates[5,6] inhibited the infection of AIDS virus in a concentration of as low as 3.3 μg/ml.[7]



ABRP (syn and anti) ADSR Si = t-butyldimethylsilyl (1→4)-β (1→4)-β

Table 1. Copolymerization of 1,4-Anhydro-2,3-O-benzylidene-α-D-ribopyranose (ABRP) with 1,4-Anhydro-2,3-di-O-t-butyldimethylsilyl-α-D-ribopyranose(ADSR)

No.[a]	ABRP feed	ADSR feed		Temp	Time	Yield	$[\alpha]_D^{25}$[b]	$\bar{M}_n$[c]	ADSR unit[d] in polymer	Stereoregularity[e] %			
										ABRP		ADSR	
	g	g	mol%	°C	h	%	deg	×10⁴	mol%	1,4-β	1,5-α	1,4-β	1,5-α
1	0.50	0	0	-40	3	62.7	-60.5	4.9	0	100	0	0	0
2	0.40	0.10	13.2	-40	5	58.3	-58.6	1.6	10.5	100	0	100	0
3	0.35	0.15	20.7	-40	24	50.3	-48.2	1.3	14.6	100	0	100	0
4	0.30	0.20	28.6	-40	24	44.9	-32.4	2.2	26.6	88	12	81	19
5	0.25	0.25	37.9	-40	24	58.6	+17.5	1.2	38.2	70	30	73	27
6	0.20	0.30	47.8	-40	24	61.8	+9.5	1.2	51.8	89	11	47	53
7	0.15	0.35	59.0	-40	24	76.9	+37.5	2.0	68.3	82	18	34	66
8	0.10	0.40	71.0	-40	5	74.4	+81.8	1.9	81.2	74	26	25	75
9	0.05	0.45	84.6	-40	4	68.5	+74.4	1.6	90.9	52	48	33	67
10	0	0.50	100	-40	1.5	51.3	+64.5	5.9	100	0	0	15	85
Effects of temperature													
11	0.30	0.20	28.6	0	20	53.7	-45.4	0.9	26.1	97	3	100	0
12				-20	22	74.1	-25.9	1.1	33.9	93	7	100	0
13	0.20	0.30	47.8	0	20	56.5	-30.0	0.8	46.9	95	5	100	0
14				-20	22	60.1	-11.4	0.9	52.9	93	7	73	27
15	0.10	0.40	71.0	0	20	43.3	-8.9	0.5	75.9	95	5	100	0
16				-20	22	92.4	+33.5	1.2	82.0	83	17	61	39

a) Solvent: CH_2Cl_2, Catalyst: $SbCl_5$: 2.0 - 2.5 mol%.
b) Measured in $CHCl_3$ (c 1). c) Determined by GPC.
d) Calculated from ^1H NMR spectrum. e) Calculated from ^{13}C NMR spectrum.

In this study, it is reported for the first time that selective ring-opening copolymerization of ABRP and ADSR was accomplished by $SbCl_5$ catalyst to give completely stereoregular copolymers consisting of both benzylidenated ribopyranosidic unit and silylated ribopyranosidic ones. t-Butyldimethylsilyl group[8] was a good protecting group as well. After selective desilylation of the copolymer was carried out with fluoride ion, the benzylidene group remained intact in the resulting copolymer which was then subjected to branching reaction.

The copolymerization was carried out under high vacuum in a sealed glass ampoule as described in the previous paper.[9] The obtained polymer was purified by reprecipitation using chloroform and methanol, followed by freeze-drying from benzene.

The result of copolymerizations is summarized in Table 1. Starting monomers were synthesized by pyrolysis of D-ribose and by subsequent protection of hydroxyl groups. These monomers, ABRP and ADSR, were readily

polymerized with $SbCl_5$ at -40 °C in CH_2Cl_2 to give a stereoregular (1→4)-β-D-ribopyranan, and a polymer with mixed structure of 1,4-β-D-ribopyranose and 1,5-α-D-ribofuranose units, respectively. When in Nos. 2 and 3, 13.2 and 20.7 mol% of ADSR in the monomer feeds were used, the obtained copolymers had completely stereoregular 1,4-β-pyranosidic structure, in which ADSR units were 10.5 and 14.6 mol%, respectively. The steroregularity of copolymers decreased with increasing molar ratio of ADSR unit in the monomer feed to reach a random structure as shown in No. 9. The specific rotation of copolymers showed negative large value for a completely 1,4-β-pyranosidic structure and positive value for a mixture of 1,4-β-pyranosidic and 1,5-α-furanosidic structures. The number-avarage molecular weight ranged from 1.2×10^4 to 2.2×10^4.

In order to synthesize a 1,4-β-pyranosidic copolymer containing a larger molar ratio of ADSR units, effects of polymerization temperature were examined (Nos. 11 - 16 in Table 1). The polymerization at 0 °C (Nos. 11, 13, and 15) in various monomer feeds afforded copolymers with almost β-stereoregularity ($[\alpha]_D^{25}$ -45.4°,-30.0°,and -8.9°) which calculated from the integration value of C1 region in the ^{13}C NMR spectrum, respectively. In No. 15, 29 mol% of ABRP in the feed led to an almost complete 1,4-β-pyranosidic copolymer. At 0 °C, the molar ratio of ADSR units in the copolymer was approximately the same as that in monomer feed, indicating that the two monomers had almost equivalent monomer reactivity ratios.

Figure 1 exhibits 67.8 MHz ^{13}C NMR spectra of copolymers prepared by ring-opening copolymerization of ABRP and ADSR (29.0 : 71.0 mol%) in the feed at (A)0 °C, (B)-20 °C, and (C)-40 °C, respectively. In Fig. 1A, it was found that the C1 absorption due to 1,5-α-furanosidic structure disappeared, suggesting that a higher polymerization temperature works effectively to give 1,4-β-pyranosidic structure if other polymerization conditions are the same. Other Lewis acid catalysts, boron trifluoride etherate and phosphorus pentafluoride, were unsuitable for

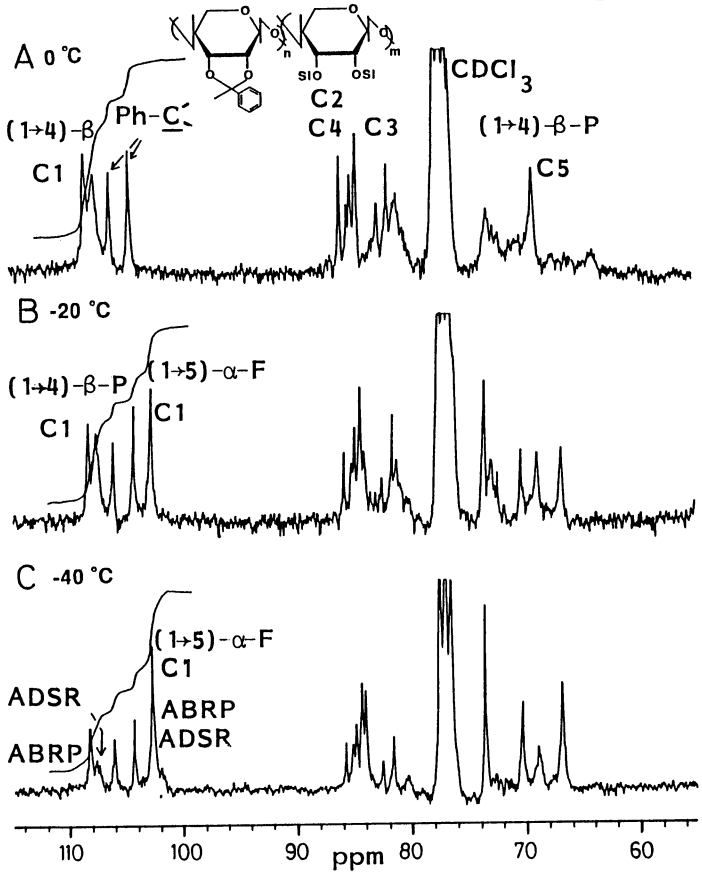


Fig. 1. 67.8 MHz ^{13}C NMR spectra of copoly(ABRP and ADSR) in $CDCl_3$. Polymerization temperature: (A) 0 °C, (B) -20°C, and (C) -40 °C. Monomer feed: ABRP : ADSR = 29.0 : 71.0 mol%.

this copolymerization, because quite low yields or no polymerization occurred.

It has been considered that the copolymerization which affords 1,4-β-pyranosidic structure with $SbCl_5$ catalyst proceeds by an oxonium ion mechanism.[2,10] In the initiation step, $SbCl_5$ first coordinates to 1,4-linked oxygen (C1-O-C4) of ABRP monomer and then the 1,4-linked oxygen of a next approaching monomer attacks to the propagating end from the backside direction of the $SbCl_5$-complexed ABRP to form an active initiating species with 1,4-β-pyranosidic structure. Similarly to ABRP, ADSR can approach from its 1,4-linked oxygen to the active species to form 1,4-β-linked copolymer backbone. In the copolymerization leading to 1,4-β-linked ribopyranose structure, the 1,4-β-linked initiating species can bind either an approaching ABRP or ADSR in such a way that the 1,4-linked oxygen of both monomers is cleaved to give both pyranose units. And this tendency is increased at a higher temperature. The reason that the 1,5-α units increased at low temperatures is assumed to be due to stabilization of an active species consisting of 1,5-α-linked ribofuranosidic unit.

Furthermore, selective desilylation with tetrabutylammonium fluoride in THF and subsequent branching with D- or L-glucose ethylorthoacetate in benzene gave a branched ribopyranan after deprotection of benzylidene groups. The free ribopyranans were sulfated with piperidine N-sulfuric acid to give branched ribopyranan sulfates with anti-AIDS viral activity. The precise results will be published elsewhere.

In conclusion, the copolymer with 1,4-β-pyranosidic structure which is the cellulose-type polysaccharide was synthesized by selective ring-opening copolymerization of ABRP and ADSR with $SbCl_5$ as catalyst at 0 ℃. The obtained copolymer is very useful to design branched ribopyranan derivatives with potent biological activities.

References

1) C. Schuerch, "Advances in Carbohydrate Chemistry and Biochemistry," ed by R. S. Tipson and D. Horton, Academic Press, Inc., New York (1981), Vol. 39, p.157; T. Uryu, "Models of Biopolymers by Ring-Opening Polymerization," ed by S. Penczek, CRC Press., Boca Raton, (1990) p.133.
2) T. Uryu, K. Kitano, K. Ito, J. Yamanouchi, and K. Matsuzaki, Macromolecules, **14**, 1 (1981).
3) Recently, it was reported that cellulose ($\bar{M}_n$ 6×10^3) was prepared from -D-cellobiosyl fluoride by cellulase catalyst: S. Kobayashi, S. Shoda, and K. Kashiwa, Polym. Prepr., Jpn., **38**, 3005 (1989).
4) T. Uryu, M. Yamanaka, M. Date, and K. Hatanaka, Macromolecules, **21**, 1916 (1988).
5) T. Yoshida, K. Hatanaka, T. Uryu, Y. Kaneko, E. Suzuki, H. Miyano, T. Mimura, O. Yoshida, and N. Yamamoto, Macromolecules, **23**, 3718 (1990).
6) K. Hatanaka, T. Yoshida, T. Uryu, O. Yoshida, H. Nakashima, N. Yamamoto, T. Mimura, and Y. Kaneko, Jpn. J. Cancer Res., **80**, 95 (1989).
7) O. Yoshida, H. Nakashima, T. Yoshida, Y. Kaneko, I. Yamamoto, K. Matsuzaki, T. Uryu, and N. Yamamoto, Biochem. Pharm., **37**, 2887 (1988).
8) G. H. Hakimelahi, Z. A. Proba, and K. K. Ogilvie, Tetrahedron Lett., **1981**, 4775.
9) C. Schuerch and T. Uryu, Macromol. Synth., **4**, 151 (1972).
10) T. Uryu, J. Yamanouchi, T. Kato, S. Higuchi, and K. Matsuzaki, J. Am. Chem. Soc., **105**, 6865 (1983).

(Received December 20, 1990)