Note

Polymerization of 1,2-anhydro-3,4-di-*O*-benzyl-*β*-L-rhamnopyranose

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L-Rhamnose is widely distributed in nature and is commonly found as a structural unit in glycolipids [1,2] and bacterial polysaccharides [3,4] and as a constituent of glycosides [5]. It is of interest to study the polymerization of 1,2-anhydro-3,4-di-*O*-benzyl-*β*-L-rhamnopyranose (Scheme 1) because α-(1 → 2)-linked rhamnopyranan, an important model compound for polysaccharide research, can be obtained from debenzylation of the resultant polymer. The syntheses of α-(1 → 2)-linked mannopyranan [6,7] and *β*-(1 → 2)-linked glucopyranan [8] have been reported by Schuerch's group. Previously we reported the synthesis of 1,2-anhydro-3,4-di-*O*-benzyl-*β*-D-, and -L-rhamnopyranose [9]. We wish to report here the polymerization of the L-form anhydride.

The 1,2-anhydro sugar was polymerized under a variety of conditions with a number of catalyst systems. The conditions and results are summarized in Table 1. Initially we used phosphorus pentafluoride as the initiator, which was a good catalyst for the polymerization of 1,6-anhydro-2,3,4-tri-*O*-benzyl-*β*-D-manno- [10] or -glucopyranose [10] and 1,2-anhydro-3,4,6-tri-*O*-benzyl-α-D-glucopyranose [8], giving high yields and excellent stereoselectivity. However, it was found in the present study that relatively low yields (44–59%) of polymer were obtained even with fairly long polymerization times. A change of solvent from dichloromethane to benzene did not improve the yield. When trifluoromethanesulfonate was used as the promoter, the polymerizations gave satisfactory yields (75–88%) but the resultant polymers were contaminated with silver which was difficult to remove. Trifluoromethanesulfonic anhydride proved to be an effective initiator of the polymerization of 1,3-anhydro-2,4,6-tri-*O*-benzyl-*β*-D-manno- [11] and

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BnO $\overline{}$ O   [OR $\overline{}$ O]

OBn   OR   O   ]$_n$
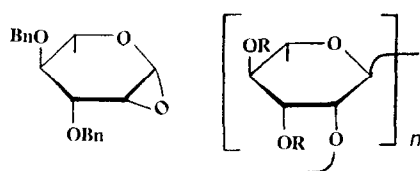
R = Bn,H, Ac

Scheme 1.

-glucopyranose [12], and also for the polymerization of 1,2-anhydro-3,4,6-tri-O-benzyl-β-D-mannopyranose [6], giving satisfactory yields and good stereoselectivity at room temperature. Thus trifluoromethanesulfonic anhydride was used as the catalyst in most of the polymerizations in the present study. It was found that polymerizations at monomer concentrations of 25–30% (monomer:solvent, g/100 mL) and catalyst amounts

Table 1
Polymerization conditions and results

	Catalyst	Mol% to monomer	Monomer to solvent ratio (g/100 mL)	Temp (deg)	Time (h)	$[\alpha]_D^{25}$ (deg)	Solvent	Yield (%)	$M_n \times 10^{-3}$	M_w / M_n
1	AgOTf	1.2	10	0	24	+15.4	CH_2Cl_2	86.7		
2	AgOTf	7.1	15	0	24	+21.1	CH_2Cl_2	85.0		
3	AgOTf	1.1	9	R	40	+11.8	CH_2Cl_2	75.5		
4	AgOTf	1.6	10	−78	40		CH_2Cl_2	86.2		
5	AgOTf	1.1	12	R	40		benzene	79.0		
6	AgOTf	1.5	11	R	4	+23.6	benzene	88.0		
7	PF_5	2.5	12	R	144	−5.3	CH_2Cl_2	42.4		
8	PF_5	1.1	10	R	144		CH_2Cl_2	59.0		
9	PF_5	1.4	28	R	144		benzene	syrup		
10	PF_5	1.4	22	R	26	−4.9	benzene	44.3		
11	$(CF_3SO_2)_2O$	1.5	26	R	0.5	−5.7	CH_2Cl_2	85.6		
12	$(CF_3SO_2)_2O$	3.1	15	R	26		CH_2Cl_2	60.7		
13	$(CF_3SO_2)_2O$	1.2	25	R	1	−10.8 (−126) [a]	CH_2Cl_2	91.3	5.0	2.1
14	$(CF_3SO_2)_2O$	0.8	24	R	4.5	−12.6	CH_2Cl_2	84.5	3.6	1.9
15	$(CF_3SO_2)_2O$	1.2	19	R	3.5		benzene	89.5		
16	$(CF_3SO_2)_2O$	1.8	29	R	0.5	−8.6	CH_2Cl_2	84.8	5.4	1.9
17	$(CF_3SO_2)_2O$	2.5	29	R	0.8	−14.9	CH_2Cl_2	88.4	5.1	2.0
18	$(CF_3SO_2)_2O$	1.9	30	R	2.5	−6.5	CH_2Cl_2	79.0	5.5	2.0
19	$(CF_3SO_2)_2O$	3.6	27	R	3	−17.5	CH_2Cl_2	93.7	4.0	1.9
20	$(CF_3SO_2)_2O$	0.7	31	R	18	−16.9	CH_2Cl_2	89.3		
21	$(CF_3SO_2)_2O$	1.9	28	R	4.5	−17.9	CH_2Cl_2	86.4		

[a] For the corresponding free polysaccharide (c 0.26).

of 0.7–3.6% (catalyst:monomer, mol%) furnished the polymers in high yields (79–93%) within a short time (usually < 5 h). Longer reaction times did not increase the yield. A change of monomer concentration from 25% to 15% decreased the polymerization yield to 61% even with long reaction times. Solvent did not affect the yield greatly; dichloromethane was used as the solvent for most of the experiments. Also, most of the polymerizations were carried out at room temperature since gelation, an indication of high yield of polymer formation, occurred at room temperature at almost the same time as it occurred at −78°.

   The resultant polymers were characterized with optical rotation, and some of them by ^{13}C NMR spectrometry, gel permeation chromatography. Some products were debenzylated and acetylated prior to characterization.

   The optical rotations of the polymers obtained with silver trifluoromethanesulfonate as the catalyst had positive signs differed from the behavior of polymers obtained with the other initiators, perhaps because of contamination by silver. Most of the benzylated polysaccharides gave optical rotation values ranging from −5 to −18°. Molecular weights and their distribution were obtained for several representative samples by gel permeation chromatography. It was found that samples 16, 17, and 18 (Table 1) gave similar molecular weights M_n (5.4, 5.1, and 5.5 × 10^3, respectively), and similar molecular-weight distributions (M_w/M_n = 1.9, 2.1, and 1.9, respectively). These results indicate little influence of reaction time on the molecular weight. Sample 19 gave a lower molecular weight, indicating that a high concentration of catalyst decreases the molecular weight. Sample 13 obtained with a catalyst concentration of 1.2% gave similar results ($M_n = 5.5 \times 10^3$, $M_w/M_n = 2.1$). The ^{13}C NMR spectrum of sample 13 gave a C-1 signal at δ 100.7 and a C-6 signal at δ 18.0, respectively, and showed major peaks for C-5 at δ 68.5, C-2 at δ 80.5, and C-3 and C-4 at δ 78.8 and δ 74.9 (assignments may be reversed). Only the C-1 and C-6 signals were singlets whereas the remaining carbons gave some small signals surrounding the major ones. This behavior may be caused either by end group effects or by the presence of β-linkages which was difficult to confirm at this stage. The signals at δ 75.4 and 72.1 were assigned as benzyl methylene carbons, and the peaks at δ 138.5, 138.2 (quaternary), and at δ 128.4, 128.3, 128.1, 127.9, 127.6 (tertiary) were designated as benzene ring carbons by the DEPT technique. Sample 11 gave the same spectrum as 13.

   It was difficult to determine whether the synthetic benzylated rhamnopyranans (Scheme 1) obtained only α-linkages from their ^{13}C NMR spectra, and thus further structural analysis was carried out. Debenzylation of sample 13 with sodium in liquid ammonia [13] followed by neutralization with Amberlite IR-120(H$^+$) ion-exchange resin furnished free rhamnopyranan (Scheme 1). The ^{13}C NMR spectrum of the free rhamnopyranan did not show signals in the aromatic region, thus indicating complete debenzylation. Six sharp peaks at δ 100.3, 76.9, 72.5, 70.5, 68.4, and 17.5 indicated a high stereoregularity of the rhamnopyranan (see Fig. 1). Signal assignments were made by comparison to spectral data for methyl α-L-rhamnopyranosyl-(1 → 2)-α-L-rhamnopyranoside [14] and methyl α-L-rhamnopyranoside [15]. It was easy to assign the signal at δ 100.3 as C-1, and the signal at δ 17.5 as C-6, and also the signal at δ 76.9 (5.9 ppm downfield shift compared to the C-2 of methyl α-L-rhamnopyranoside) as C-2. The signals at δ 68.4, 72.5, and 70.5 were assigned as C-5, C-4, and C-3, respectively,
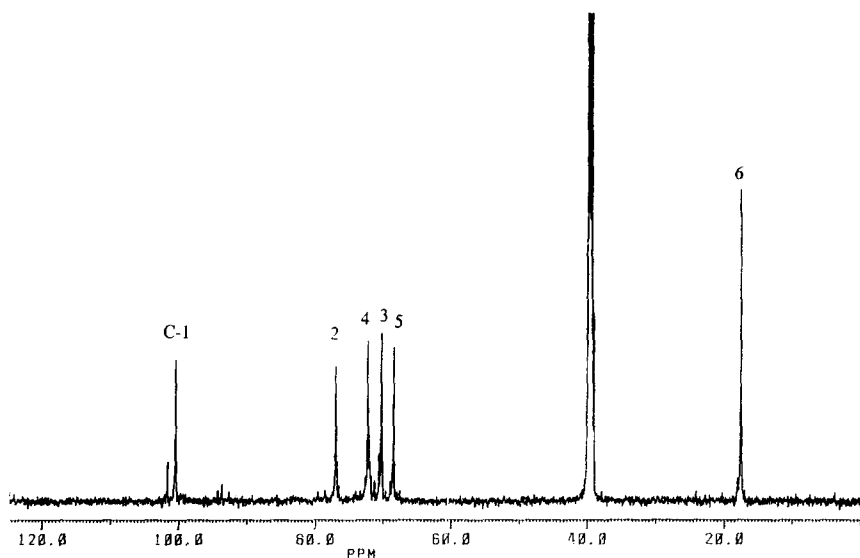
Fig. 1. The ^{13}C NMR spectrum of synthetic α-(1 → 2)-linked rhamnopyranan.

based on the relative order of chemical shifts for the three carbons in either mono- [15] or di-saccharide [14] (see Table 2). The value of $^1J_{\text{C-1,H-1}}$ (170 Hz) unambiguously indicated an α-linkage at C-1 based on the reported data for α-L-rhamnopyranosides ($^1J_{\text{C-1,H-1}}$ 164–168 Hz) and for β-L-rhamnopyranosides ($^1J_{\text{C-1,H-1}}$ 152–158 Hz) [16]. Measurements of $^1J_{\text{C-1,H-1}}$ for the minor peaks at δ 101.5 and 100.5 did not give a clear indication of configuration because of peak overlap. We assume that the chemical shifts of the α- and β-C-1 signals in α-(1 → 2)-linked rhamnopyranan should be similar to those in α-(1 → 2)-linked mannopyranan. The latter showed α-C-1 at δ 101.4 and β-C-1 at δ 97–100 [7]. Since no peaks were detected upfield (97–100 ppm) of the C-1 signal (100.3 ppm), the signals at δ 101.5 and 100.5 should be due to C-1 of reducing

Table 2
^{13}C NMR data (δ ppm) for benzylated (13) and free α-(1 → 2)-linked rhamnopyranan (A) in comparison with methyl α-L-rhamnopyranoside (1), and methyl α-L-rhamnopyranosyl-(1 → 2)-α-L-rhamnopyranoside (2)

	Chemical shift						
	C-1	C-2	C-3	C-4	C-5	C-6	PhCH$_2$
13	100.5	80.5	75.0 ^{a}	78.8 ^{a}	68.5	17.9	72.1, 75.4
A	100.3	76.9	70.5	72.5	68.4	17.5	
1	101.9	71.0	71.3	73.1	69.4	17.7	
2	100.5	79.0	70.9	73.1	69.2	17.7 (reducing end)	
	102.9	71.1	70.9	72.9	69.7	17.8 (non-reducing end)	

^{a} May be exchangeable.

Table 3
^{1}H NMR data (δ ppm) for acetylated α-(1 → 2)-linked rhamnopyranan (AcA), methyl α-L-rhamnopyranosyl-(1 → 2)-α-L-rhamnopyranoside (α, α) and methyl β-L-rhamnopyranosyl-(1 → 2)-α-L-rhamnopyranoside (β, α)

	Chemical shift					
	H-1 (H-1′)	H-2 (H-2′)	H-3 (H-3′)	H-4 (H-4′)	H-5 (H-5′)	H-6 (H-6′)
AcA	4.95	4.13	5.25	5.03	3.88	1.23
α, α	4.79	3.94	3.83	3.47	3.68	1.32
	(4.98)	(4.08)	(3.81)	(3.46)	(3.76)	(1.29)
β, α	4.84	4.12	3.76	3.49	3.71	1.34
	(4.74)	(4.06)	(3.63)	(3.39–3.48)	(3.39–3.48)	(1.34)

and/or non-reducing ends (α-linkage). The ratio of the major C-1 peak to either of the two small peaks was around 7:1, indicating a degree of polymerization (dp) of 14. Several small peaks were observed at δ 76.8 near C-2, 72.0 near C-4, and 70.6 near C-3, respectively, but it was difficult to assign them. ^{1}H NMR of the synthetic rhamnopyranan in deuterated Me$_2$SO did not give a good spectra even at an elevated temperature. Thus acetylation of the polysaccharide with acetic anhydride in formamide was conducted, affording a fully acetylated α-(1 → 2)-L-rhamnopyranan (Scheme 1). Its ^{1}H NMR spectrum showed major peaks for H-1 at δ 4.95 (bs), H-2 at δ 4.13 (t, $J_{1,2} = J_{2,3} = 3$ Hz), H-3 at δ 5.25 (dd, $J_{2,3}$ 3, $J_{3,4}$ 10 Hz), H-4 at δ 5.03 (t, $J_{3,4} = J_{4,5} = 10$ Hz), H-5 at δ 3.88 (m), and H-6 at δ 1.23 (d, $J_{5,6}$ 6 Hz). It was reported that the difference between α-H-1′ (δ 4.98) of methyl α-L-rhamnopyranosyl-(1 → 2)-α-L-rhamnopyranoside and β-H-1′ (δ 4.74) of methyl β-L-rhamnopyranosyl-(1 → 2)-α-L-rhamnopyranoside [17], and the difference between α-H-5′ (δ 3.76) and β-H-5′ (3.39–3.48), were 0.25 and 0.32 ppm, respectively (see Table 3). However, no peaks were detected upfield of H-5 (2.62–3.88 ppm) and upfield of H-1 (4.20–4.80 ppm) in the ^{1}H NMR spectrum, again indicating virtually complete α-linkage in the polymer. As observed in the ^{13}C NMR spectrum, several small peaks representing reducing or non-reducing end ring protons were also observed (at δ 5.48, 5.37, 5.32, etc.) and the ratio of minor peak:major peak for each set was also around 1:7.

In summary, 1,2-anhydro-3,4-di-O-benzyl-β-L-rhamnose was polymerized with trifluoromethanesolfonic anhydride as the initiator in dichloromethane at room temperature. Debenzylation with sodium in liquid ammonia afforded free α-(1 → 2)-linked rhamnopyranan that was identified by ^{13}C and ^{1}H NMR spectrometry, in the latter case using the acetylated polysaccharide.

1. Experimental

General methods.—^{13}C NMR spectra of free rhamnan were obtained in dimethyl-d_6 sulfoxide and ^{1}H NMR spectra of the acetylated polysaccharide were obtained in chloroform-d with a Varian XL-500 spectrometer at room temperature or at 40 °C. ^{13}C

NMR spectra of benzylated polymers were obtained with a Varian XL-200 spectrometer in chloroform-*d* with tetramethylsilane as the internal standard. Optical rotations were determined in chloroform for benzylated polysaccharides, and in Me_2SO for the free polysaccharides at 20 °C using a Perkin–Elmer Model 241-MC polarimeter with a jacketed 1-dm cell. Molecular-weight distributions of the substituted polysaccharides were obtained by high-pressure gel-permeation chromatography in tetrahydrofuran. A Waters model 208 chromatograph equipped with a UV detector and a Valvco septumless injector (1.0 mL) was used. A stainless steel column (30 cm) packed with μ-Styragel (500A) was used for the analysis at a flow rate of 1.0 mL/min. A calibration curve was made using polystyrene (Waters) standard samples.

Monomer synthesis.—1,2-Anhydro-3,4-di-*O*-benzyl-β-L-rhamnopyranose was synthesized and purified as described previously [9]. $[\alpha]_D^{20}$ +9.7 (*c* 0.85, $CHCl_3$) [9]. $[\alpha]_D^{23}$ +5.1 (*c* 0.78 $CHCl_3$); mp 103 °C [9]. mp 100 °C.

Polymerization of 1,2-anhydro-3,4-di-O-benzyl-β-L-rhamnopyranose.—The transfer of the catalysts and solvents, and all the polymerizations were performed under high-vacuum conditions as reported previously [18]. The polymerization conditions are summarized in Table 1. Polymerizations were terminated by the addition of dry methanol. The precipitated polymers were dissolved in chloroform, washed with water, and poured into petroleum ether. The polymers were freezed dried from benzene.

Preparation of (1 → 2)-α-L-rhamnopyranan.—Polymer 13 (Table 1) (350 mg) was dissolved in toluene and the solution was stirred with liquid ammonia as described for related debenzylations. Freshly cut sodium metal was added slowly. After the characteristic blue color had remained for 3 h, the ammonia was removed in a stream of nitrogen, and the residue dissolved in water. The solution was carefully neutralized with Amberlite IR-120 (H^+ form) ion-exchange resin. The free rhamnopyranan was obtained quantitatively as a fluffy solid by freeze-drying from distilled water.

Acetylation of (1 → 2)-α-L-rhamnopyranan.—The free rhamnopyranan (25 mg) was thoroughly mixed with formamide (0.5 mL) in a 50 mL flask. To this stirred solution were slowly added dry pyridine (6 mL) and acetic anhydride (4 mL). The reaction mixture was stirred overnight at room temperature. The reaction mixture was then slowly added to ice–water (40 mL) with stirring. Extraction with chloroform was repeated several times and the organic solution was decolorized with activated carbon and concentrated to 2 mL. Reprecipitation was repeated five times into petroleum ether to remove pyridine and a white fluffy polymer was obtained by freeze-drying from benzene.

References

[1] S.N. Khanna and P.C. Gupta, *Phytochemistry*, 6 (1967) 735–741.
[2] F.G. Jarvis and M.J. Johnson, *J. Am. Chem. Soc.*, 71 (1949) 4124–4130.
[3] B. Lindberg, J. Lönngren, J.L. Thompson, and W. Nimmich, *Carbohydr. Res.*, 25 (1972) 49–61.
[4] Y.N. Choy and G.G.S. Dutton, *Can. J. Chem.*, 52 (1974) 684–692.
[5] H. Wagner, M. Ertan, and O. Seligmann, *Phytochemistry*, 13 (1974) 857–864.
[6] D.L. Trumbo and C. Schuerch, *Carbohydr. Res.*, 135 (1985) 195–202.
[7] H. Yamaguchi and C. Schuerch, *Biopolymers*, 19 (1980) 297–309.

[8] P.F. Sharkey, R. Eby, and C. Schuerch, *Carbohydr. Res.*, 96 (1981) 223–229.

[9] Q. Chen and F. Kong, and L. Cao, *Carbohydr. Res.*, 240 (1993) 107–117.

[10] C. Schuerch, *Adv. Carbohydr. Chem. Biochem.*, 39 (1981) 157–212.

[11] F. Kong and C. Schuerch, *Macromolecules*, 17 (1984) 983–989.

[12] F. Good and C. Schuerch, *Macromolecules*, 18 (1985) 595–600.

[13] P. Kovác and S. Bauer, *Tetrahedron Lett.*, (1972) 2349–2350, and references therein.

[14] A. Lipták, A. Neszmélyi, and H. Wagner, *Tetrahedron Lett.*, (1979) 741–744.

[15] P.A.J. Gorin and M. Mazurek, *Can. J. Chem.*, 53 (1975) 1213–1223.

[16] R. Kasai, M. Okihara, J. Asakawa, K. Mizutani, and O. Tanaka, *Tetrahedron*, (1979) 1427–1432.

[17] S.S. Mamyan, G.M. Lipkind, A.S. Shashkov, N.E. Bairamova, A.V. Nikolaev, and N.K. Kochetkov, *Bioorg. Khim.*, 14 (1988) 205–215.

[18] H. Ito and C. Schuerch, *Macromolecules*, 14 (1981) 246–249.