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Synthesis of Poly[(1→6)-2,5-Anhydro-D-Glucitol] by Cationic Cyclopolymerization of 3,4-Di-*O*-Allyl-1,2:5,6-Dianhydro-D-Mannitol

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SYNTHESIS OF POLY[(1→6)-2,5-ANHYDRO-D-GLUCITOL] BY CATIONIC CYCLOPOLYMERIZATION OF 3,4-Di-*O*-ALLYL-1,2:5,6-DIANHYDRO-D-MANNITOL

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ABSTRACT

The cyclopolymerization of 3,4-di-*O*-allyl-1,2:5,6-dianhydro-D-mannitol (**1d**) using BF_3·OEt_2 produced poly[(1→6)-3,4-di-*O*-allyl-2,5-anhydro-D-glucitol] (**2d**). For the polymerization in CH_2Cl_2 at -10 °C,

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the maximum yield and M_n were obtained as 58.9 % and 4890, respectively. The specific rotations ($[\alpha]^{22}_{546}$) of the obtained polymers were +34.0° ~ +38.8° (c=1.0 in $CHCl_3$). The deallylation of polymer **2d** in acetic acid/ethanol/water using the Pd-C catalyst perfectly proceeded to form poly[(1→6)-2,5-anhydro-D-glucitol] (**3**). The specific rotations ($[\alpha]^{22}_{546}$) of the resulting polymers were +17.1° ~ +18.9° (c=1.0 in H_2O). Polymer **2d** was soluble in chloroform and tetrahydrofuran, but insoluble in water, whereas polymer **3** was soluble in water but insoluble in chloroform and tetrahydrofuran.

INTRODUCTION

Recently, we reported that 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol (**1a-c**) was polymerized using BF_3·OEt_2 to form a polymer consisting of 3,4-di-*O*-alkyl-2,5-anhydro-D-glucitol as the cyclic constitutional repeating unit, i.e., poly[(1→6)-3,4-di-*O*-alkyl-2,5-anhydro-D-glucitol] (**2a-c**) [1-4]. In the host-guest complexation, polymer **2** acted as a macromolecular ionophore which formed complexes with such organic cations as methylene blue and rhodamine 6G along with alkali metal picrates [1]. Polymer **2** also showed the chiral recognition ability for the racemic α-amino acid. The structural characteristic of **2** is the lack of the anomeric proton, which exactly differs from the naturally occurring polysaccharides [3,4]. Therefore, **2** is a novel, synthetic carbohydrate polymer, and poly[(1→6)-2,5-anhydro-D-glucitol] (**3**) should be a useful precursor for producing the derivatives with various substituents at the 3,4-di-*O*-positions. Here we report that poly[(1→6)-3,4-di-*O*-allyl-2,5-anhydro-D-glucitol] (**2d**) is synthesized using the cationic cyclopolymerization of 3,4-di-*O*-allyl-

1,2:5,6-dianhydro-D-mannitol (**1d**), and **3** is then prepared with the cleavage of the allyl ether linkage in **2d**.

EXPERIMENTAL

Synthesis of the monomer

3,4-Di-*O*-allyl-1,2:5,6-dianhydro-D-mannitol (**1d**) was prepared from D-mannitol by the known method [6]. b.p.$_{0.2}$ 98 ~ 101 °C [Lit. [6], b.p.0.3 112 ~ 115 °C]; $[\alpha]_D$ = +7.1° , $[\alpha]_{546}$ = +7.3° (c=1.0, $CHCl_3$ at 22 °C)[Lit.[6]), $[\alpha]^{20}_D$ = 0 (c=1.0, $CHCl_3$)]; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.84-5.96 (m, 2H, -CH=), 5.26 (ddd, *J* =17.3, 3.1, and 1.5 Hz, 2H, trans $=CH_2$), 5.19 (ddd, *J* =10.3, 2.6, and 1.2 Hz, 2H, cis $=CH_2$), 4.04-4.24 (m, 4H, -C*H*$_2$CH=), 3.35-3.39 (m, 2H, -C*H*-OCH$_2$CH=), 3.14-3.18 (m, 2H, -OCH$_2$C*H*-), 2.87 (dd, *J* =5.3 and 3.9 Hz, 2H, cis -OC*H*$_2$CH-), 2.78 (dd, *J* =5.3 and 2.6 Hz, 2H, trans -OC*H*$_2$CH-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.71 (-CH=), 117.46 (=CH_2), 78.42 (-*C*H-OCH$_2$CH=), 72.41 (-*C*H$_2$CH=), 50.35 (-OCH$_2$*C*H-), and 46.35ppm (-O*C*H$_2$CH-).

Synthesis of the polymers

***Typical procedure for the synthesis of poly[(1→6)-3,4-di-O-allyl-2,5-anhydro-D-glucitol] (2d)*:** To a solution of **1d** (0.5 g, 2.21 mmol) in dry CH_2Cl_2 (4.43 mL) was added a solution (0.739 mol•L^{-1}) of BF_3•OEt_2 in CH_2Cl_2 (30.1 μL, 0.0221 mmol) at 0 °C using a microsyringe. After 2 h, the reaction mixture was poured into methanol which contained a drop of aqueous ammonia, and the entire solution was evaporated under reduced pressure. The residue was washed several times with *n*-hexane and then it was dried under vacuum to yield the polymer (232 mg, yield 46.4 %). The M_n and M_w/M_n were 4220 and 1.98, respectively. $[\alpha]_D$ = +29.1°, $[\alpha]_{577}$ = +32.0°, $[\alpha]_{546}$ = +36.3°,

$[\alpha]_{435}$ = +61.8°, and $[\alpha]_{405}$ = +73.7° (c=1.0, $CHCl_3$ at 22 °C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.45 (-CH=), 116.88 and 117.14 ($=CH_2$), 83.75 (CH), 82.48 (CH), 79.88 (CH), 71.73 (CH_2), 70.40 and 70.52 (-CH_2CH=), and 69.30 ppm (CH_2).

Typical procedure for the synthesis of poly[(1→6)-2,5-anhydro-D-glucitol] (3): A stirred solution of polymer **2d** (0.58 g) in ethanol (8 mL), acetic acid (1 mL), and water (8 mL) under argon was boiled in the presence of 10 % Pd-C catalyst (0.5 g). After 10 h, the catalyst was filtered off, and the filtrate was evaporated. Ethanol was then added to and evaporated from the residue, and this procedure was repeated three times. The residue was purified using reprecipitation from methanol/tetrahydrofuran. $[\alpha]_D$ = +9.9°, $[\alpha]_{577}$ = +11.8°, $[\alpha]_{546}$ = +13.2°, $[\alpha]_{435}$ = +24.1°, and $[\alpha]_{405}$ = +29.6° (c=1.0, H_2O). ^{13}C NMR (100 MHz, D_2O): δ = 86.11 (CH), 82.45 (CH), 81.12 (CH_2), 79.80 (CHOH), 74.12 (CH_2), and 72.41 ppm (CH_2).

Synthesis of the cyclic compounds

3,4-Di-O-allyl-2,5-anhydro-D-glucitol (4d): The mixture of 1.75 g (10 mmol) of **1d** and 40 mL of water was heated under reflux for 7 h. After cooling, the solution was evaporated under reduced pressure to a syrup from which the water was removed using azeotropic distillation with benzene and chloroform twice. A syrupy mixture was separated using flush column chromatography with ethyl acetate/isopropanol (5/1) as the eluent. The fractions having R_f 0.5 produced, upon evaporation, **4d** as a syrup (1.60 g, 82 %). $[\alpha]_D$ = +55.9°, $[\alpha]_{577}$ = +60.0°, $[\alpha]_{546}$ = +69.2°, $[\alpha]_{435}$ = +115.7°, and $[\alpha]_{405}$ = +138.3° (c=1.0, $CHCl_3$ at 22 °C). ^1H NMR (400 MHz, $CDCl_3$): δ = 5.82-5.95 (m, 2H, -CH=), 5.30 (ddt, J_{trans}=17.3 Hz, J_{gem}=4.9 Hz, $^4J_{vic}$=1.6 Hz, 2H, trans $=CH_2$), 5.23 (ddt,

J_{cis}=10.4 Hz, J_{gem}=4.3 Hz, $^4J_{vic}$=1.4 Hz, 2H, cis =CH_2), 3.82-4.19 (m, 4H of -C*H*$_2$CH= and unsolved 7H), 3.70 (dd, *J*=11.9 and 4.1 Hz, 1H, unsolved), and 2.23 ppm (br. s, 2H, -OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.11 and 133.69 (-CH=), 117.90 and 117.55 (=CH_2), 83.92 and 83.63 (-*C*H-OCH$_2$CH=), 82.64 and 80.28 (CH), 71.00 and 70.76 (-*C*H$_2$CH=), and 62.84 and 61.77 ppm (-CH_2OH). FI-MS m/z (relative intensity) 243 (9.3), 244 (M+-91.6), 245 (MH+-100), 246 (20.9), 489 ((2M+H)+-23.0), and 490 (8.5). Elemental analysis for $C_{12}H_{20}O_5$ (%): Calculated C 59.00, H 8.25; found C 59.01, H 8.25.

3,4-Di-O-allyl-2,5-anhydro-1,6-di-O-methyl-D-glucitol (5d): To a stirred solution of 0.96 g (5 mmol) of **4d** in 6.4 mL of dimethyl sulfoxide were simultaneously added a solution of 1 g of sodium hydroxide in 1 mL of water and 1.60 g (12.6 mmol) of dimethyl sulfate, and the temperature of the reaction mixture did not exceed 60 °C. Stirring was continued at this temperature for 30 min. After standing overnight at room temperature, the mixture was poured into water and extracted with chloroform. The extract was dried and evaporated, and the residue was separated using a column chromatography with ether/*n*-hexane (1/1) as the eluent. The fractions having R_f 0.45 produced, upon evaporation, **5d** as a colorless liquid (0.55 g, 50 %). $[\alpha]_D$ = +46.2°, $[\alpha]_{577}$ = +48.3°, $[\alpha]_{546}$ = +54.3°, $[\alpha]_{435}$ = +90.8°, and $[\alpha]_{405}$ = +108.1° (c=1.0, $CHCl_3$ at 22 °C). ^{1}H NMR(400 MHz, $CDCl_3$): δ = 5.82-5.95 (m, 2H, -CH=), 5.29 (ddt, *J*trans=17.2 Hz, *J*gem=4.7 Hz, $^4J_{vic}$=1.6 Hz, 2H, trans =CH_2), 5.20 (ddt, J_{cis}=10.4 Hz, *J*gem=4.7 Hz, $^4J_{vic}$=1.5 Hz, 2H, cis =CH_2), 3.80-4.17 (m, 4H of -C*H*$_2$CH= and unsolved 4H), 3.58-3.67 (m, 2H), 3.54 (dd *J*=10,1 and 6,1 Hz, 1H, unsolved). 3.47 (dd *J*=10.1 and 6.1 Hz, 1H, unsolved), and 3.39 ppm (s, 6H, -OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.13 (-CH=), 117.89 and 117.64 (=CH_2), 84.36 (C4),

83.16 (C3), 82.30 (C2), 79.74 (C5), 73.89 (C1), 71.40 (C6), 71.39 (-CH_2CH=), and 59.91 ppm (-OCH_3). FI-MS m/z (relative intensity) 272 (M+-100), 273 (27.5), 274 (6.9), and 545 ((2M+H)+-4.1). Elemental analysis for $C_{14}H_{24}O_5$ (%): Calculated C 61.74, H 8.88; found C 61.60, H 9.06.

Measurements

^1H and ^{13}C NMR spectra were recorded with a Brucker MSL 400 instrument. Optical rotation measurements were made with a Jasco DIP-140 digital polarimeter. The molecular weight of the resulting polymers were measured using gel permeation chromatography (GPC) in tetrahydrofuran on a WATERS M45 high-performance liquid chromatograph equipped with three polystyrene gel columns (Shodex KF-804L).

RESULTS AND DISCUSSION

For the polymerization of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol (**1a-d**) [1-4], BF_3•OEt_2 was a suitable initiator for producing poly[(1→6)-3,4-di-*O*-alkyl-2,5-anhydro-D-glucitol]. Table 1 lists several results of the polymerization of 3,4-di-*O*-allyl-1,2:5,6-dianhydro-D-mannitol (**1d**) using BF_3•OEt_2. The entire polymerization homogeneously proceeded and the polymers were sticky semi-solids that were soluble in methanol, chloroform, and tetrahydrofuran and insoluble in water and *n*-hexane. The yields and the number-averaged molecular weights (M_n) for the polymers obtained in CH_2Cl_2 were higher than those in $C_2H_5NO_2$. For the polymerization in CH_2Cl_2 at -10 °C, the maximum yield and M_n were obtained as 58.9 % and 4890, respectively.

Table 1 . Cyclopolymerization of 3,4-di-*O*-allyl-1,2:5,6-dianhydro-D-mannitol (**1d**) with BF_3•OEt_2 a)

Run no.	Solvent	Temp. ℃	Yield %	M_n b)	M_w/M_n b)	$[\alpha]_{546}^{22}$ c)
1	CH_2Cl_2	0	46.4	4220	1.98	+36.9
2	CH_2Cl_2	-10	58.9	4890	1.60	+34.0
3	$C_2H_5NO_2$	0	47.2	3570	1.38	+35.9
4	$C_2H_5NO_2$	-10	39.5	2640	1.32	+38.8

a) [**1d**]=0.5 mol•L^{-1}; [**1d**]/[BF_3•OEt_2]=100; time, 2 h.

b) Measured in THF by GPC using poly(styrene) as standard.

c) c=1.0, $CHCl_3$.

The specific rotations ($[\alpha]^{22}_{546}$) of the polymers obtained were +34.0°~38.8° (c=1.0 in $CHCl_3$).

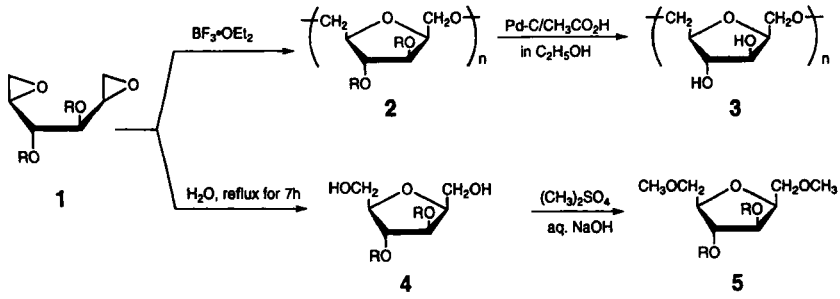
Figures 1a and 2b show the ^{13}C and ^{1}H NMR spectra of the polymer prepared from **1d**. Because the characteristic signals due to the epoxy carbons (46.35 and 50.35 ppm) and protons (2.75-2.87 and 3.15-3.20 ppm) disappeared, the polymer essentially consisted of cyclic constitutional repeating units caused by the cyclopolymerization mechanism, i.e., the extent of cyclization is 100 %.

Previously, the cyclic constitutional repeating units in the polymers (**2a-c**) from 3,4-di-*O*-alkyl-2,5-anhydro-1,6-di-*O*-methyl-D-mannitol (**1a-c**) were provided by comparing their ^{13}C NMR spectra with those of 3,4-di-*O*-alkyl-2,5-anhydro-D-mannitol (**3a-c**) [1,2], which were

synthesized from **1** as shown in Scheme 1. In order to confirm the cyclic units in the polymer from **1d**, 3,4-di-*O*-allyl-2,5-anhydro-1,6-di-*O*-methyl-D-glucitol (**5d**) was also prepared by the procedure similar to that described by Wiggins et. al.[5]. Figure 1 shows the ^{13}C NMR spectra of the polymers from **1d** and **5d**. The signals at 83.75, 82.48 (the intensity of this signal is double for those of the other two), and 79.88 ppm for the polymer were very close to those at 84.36, 83.16, 82.30, and 79.74 ppm which were assigned to the carbons of C4, C3, C2, and C5, respectively, for **5d**. This result concluded that the cationic cyclopolymerization of **1d** is regio- and stereospecific to produce 1→6 bonded 3,4-di-*O*-allyl-2,5-anhydro-D-mannitol as the 5-membered constitutional repeating unit, i.e., polymer **3**.

The cleavage of the allyl ether linkage in polymer **2d** was completed with a Pd-C catalyst in ethanol/acetic acid under an Ar atmosphere. For the polymers with lower M_ns (Run no. 3 and 4), the yields were lower than those for Run no. 1 and 2. The lower yield was caused by removing the lower molecular weight part through the reprecipitation procedure. In the ^1H NMR spectrum of the resulting polymer (Figure 2a), the characteristic signals at 5.8-5.9 and 5.2-5.3 ppm due to the allylic protons of =CH and $=CH_2$, respectively, completely disappeared. This result indicates that the cleavage of the allyl ether linkage perfectly proceeds and polymer **3** consists of the 2,5-anhydro-D-glucitol unit, i.e., poly[(1→6)-2,5-anhydro-D-glucitol]. The specific rotations ($[\alpha]^{22}_{546}$) of the polymers obtained were +17.1° ~ +18.9° (c=1.0 in H_2O).

The solubility of poly[(1→6)-2,5-anhydro-D-glucitol] (**3**) is different from that of poly[(1→6)-3,4-di-*O*-allyl-2,5-anhydro-D-glucitol]



1a, 2a, 4a, 5a; R= -CH_3
1b, 2b, 4b, 5b; R= -CH_2CH_3
1c, 2c, 4c, 5c; R= -$(CH_2)_4CH_3$
1d, 2d, 4d, 5d; R= -$CH_2CH{=}CH_2$

Scheme 1

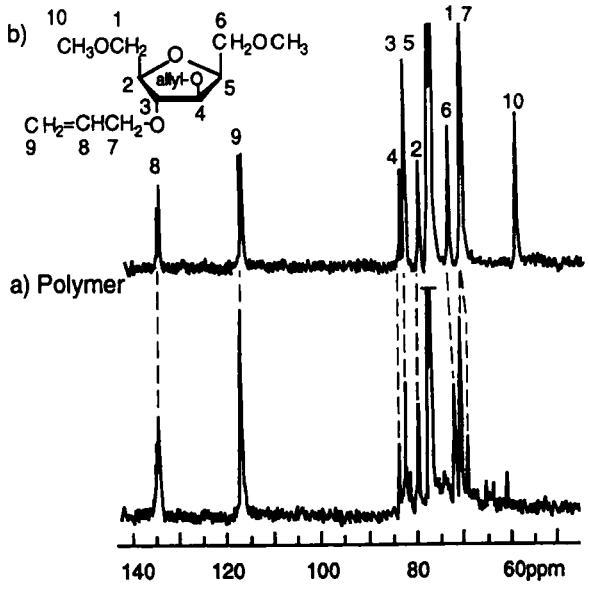


Figure 1. ^{13}C NMR (100 MHz, $CDCl_3$) spectra of polymer **2d** (a) and 3,4-di-*O*-allyl-2,5-anhydro-D-glucitol (**5d**) (b).

Table 2. Synthesis of poly[(1→6)-2,5-dianhydro-D-glucitol] (**3**) by deallylation of poly[(1→6)-3,4-di-*O*-allyl-2,5-dianhydro-D-glucitol] (**2d**) with Pd-C catalyst in acetic acid/ethanol/water [a]

2d [b]	**3**	
	Yield	$[\alpha]_{546}^{22}$ [c]
	%	
1	47.8	+17.1
2	60.3	+18.9
3	28.7	+17.7
4	30.1	+17.3

a) Typical procedure was described in the experimental section.

b) The number of 1, 2, 3, and 4 for **2d** correspond to the polymers obtained from the polymerizations of Run no. 1, 2, 3, and 4 in Tabel 1, respectively.

c) c=1.0, H_2O.

(**2d**) as summarized in Table 3. Polymer **2d** is soluble in methanol, chloroform, and tetrahydrofuran and insoluble in water and *n*-hexane; whereas, polymer **3** is soluble in water and methanol but insoluble in *n*-hexane, chloroform, and tetrahydrofuran. After the cleavage of the allyl groups from polymer **2d**, polymer **3** was easily purified using reprecipitation from methanol/tetrahydrofuran.

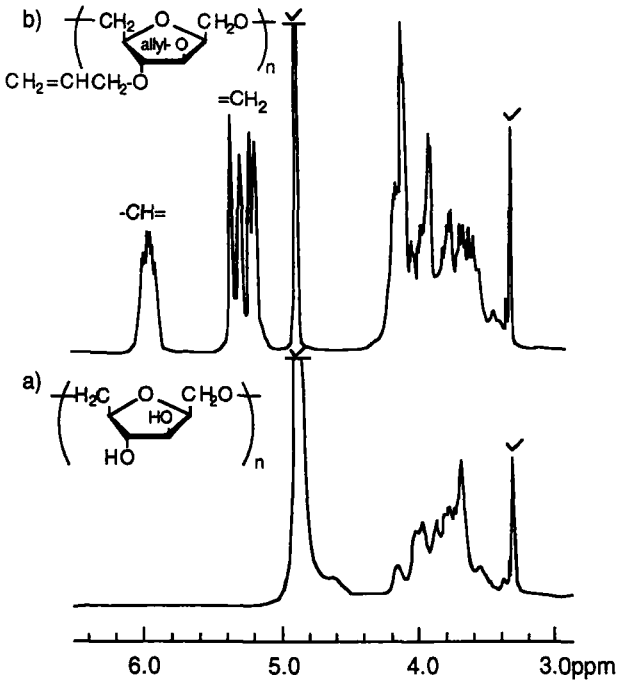


Figure 2. ^{1}H NMR (400 MHz, CD_3OD) spectra of polymer **3** (a) and polymer **2d** (b).

Table 3. Solubility of poly[(1→6)-3,4-di-*O*-allyl-2,5-dianhydro-D-glucitol] (**2d**) and poly[(1→6)-2,5-dianhydro-D-glucitol] (**3**)

	H_2O	MeOH	*n*-Hexane	$CHCl_3$	THF
2d	×	○	×	○	○
3	○	○	×	×	×

In summary, we prepared poly[(1→6)-2,5-anhydro-D-glucitol] using the synthesis and deallylation of poly[(1→6)-3,4-di-*O*-allyl-2,5-anhydro-D-glucitol], which was obtained using the cationic cyclopolymerization of 3,4-di-*O*-allyl-1,2:5,6-dianhydro-D-mannitol. Further study is underway to investigate the synthesis and immunomodulating application of poly[(1→6)-2,5-anhydro-3,4-di-*O*-sulfonyl-D-glucitol].

REFERENCES

[1] H. Hashimoto, T. Kakuchi, K. Yokota, *J. Org. Chem.* **56**, 6470 (1991)

[2] T. Kakuchi, T. Satoh, S. Umeda, H. Hashimoto, K. Yokota, *Macromolecules*, submitted

[3] T. Kakuchi, Y. Harada, Y. Satoh, K. Yokota, H. Hashimoto, *Polymer* **35**, 204 (1994)

[4] T. Kakuchi, T. Satoh, S. Umeda, J. Mata, K. Yokota, *Chirality*, accepted.

[5] L. F. Wiggins, D. J. C. Woods, *J. Chem. Soc.*, 1566 (1950)

[6] J. Kuszmann, *Carbohyd. Res.*, **71**, 123 (1979)