Regio- and Stereoselective Cyclopolymerization of 1,2:5,6-Dianhydrohexitol

A Dissertation for the Degree of Doctor of Engineering

Hokkaido University

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Toshifumi Satoh

Contents

Chapter 3

Highly Regio- and Stereoselective Cyclopolymerization of 1,2:5,6-Dianhydro-3,4-di-*O*-alkyl-D-mannitols using Anionic Catalysts

Chapter 4

Regio- and Stereoselective Cyclopolymerization of (2*S*,5*S*)-1,2:5,6-Diepoxyhexane

Chapter 5

Cyclopolymerization of 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol to Form (6→1)-2,5-Anhydro-3,4-di-*O*-methyl-D-glucitol

Chapter 1

Introduction

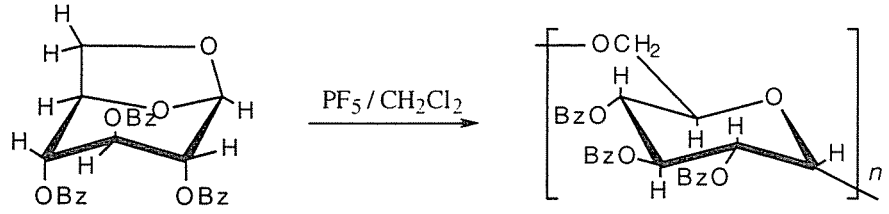
1.1 Synthesis of Polysaccharide using Polymerization without in vivo

Living organisms have structural elements with excellent mechanical properties and with unique abilities to grow, move, and reproduce. The constituent materials which carry out the functions within the organisms are primarily three kind of macromolecules, i.e. proteins, nucleic acids, and polysaccharides. The functions of proteins and nucleic acids in living tissues are widely recognized, but the roles of polysaccharides are not adequately understood. The structural polysaccharides such as chitin and cellulose are found in the major portion of the exoskeletons of insects and arthropods and of the cell walls of plants and microbes. On the other hand, the nutrient polysaccharides such as starch and glycogen are used as a energy source of life on living creatures. Recently, these polysaccharides have received considerable attention as raw materials for biomedical, antiviral, and other applications. Therefore, continuous efforts have been made in the study of chemical modification. In addition to natural polysaccharides, an investigation of synthesizing various polysaccharides without in vivo is deeply important for extending applications.

Ring-opening polymerization of an anhydro monosaccharide is an established method for preparing various types of polysaccharides.[1-17] Schuerch et al. reported that the high molecular weight 1,6-α-linked polyglucose (dextran) with the controlled backbone linkage and the complete stereoregularity, which are two major characteristics of natural

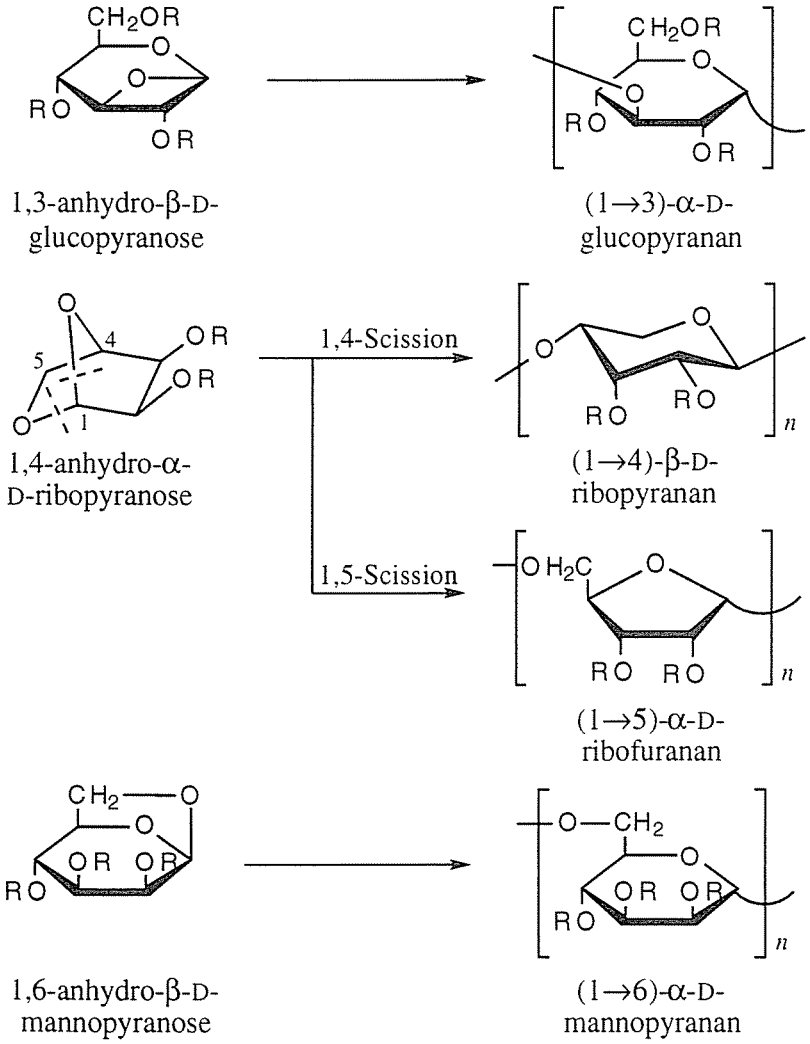
polysaccharides, was successfully synthesized by ring-opening polymerization of 1,6-anhydro-β-D-glucopyranose (Scheme 1.1).[10,11] The polyglucose was the first synthetic polysaccharide having a highly stereoregular structure similar to that of a natural polysaccharide.

Scheme 1.1



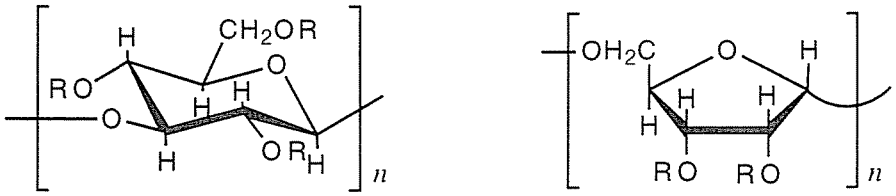
Using the ring-opening polymerization method, a new type of highly stereoregular polysaccharide was synthesized from the anhydro sugars, i.e.,

Scheme 1.2



(1→3)-α-D-glucopyranan from 1,3-anhydro-β-D-glucopyranose,[12,13] (1→4)-β-D-ribopyranan and (1→5)-α-D-ribofuranan from 1,4-anhydro-α-D-ribopyranose,[15,16] and (1→6)-α-D-mannopyranan from 1,6-anhydro-β-D-mannopyranose (Scheme 1.2).[17] These polysaccharides are termed artificial polysaccharides. These polysaccharides exhibit biological activity,[18] and, in particular, the sulfated ones are widely noticed in terms of an inhibitory effect towards AIDS (Acquired Immunodeficiency Syndrome) (Scheme 1.3).[19-22]

Scheme 1.3

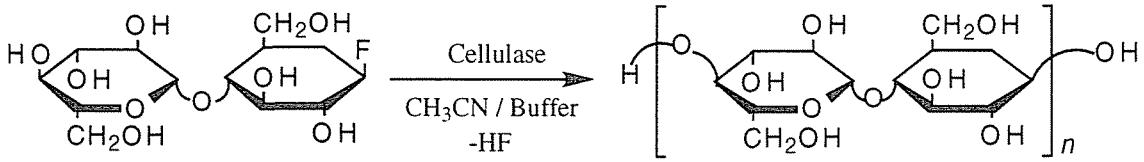


R: -SO_3Na or -H

Curdlan sulfate Ribofuranan sulfate

Polysaccharides existing the most abundantly in nature are 1,4-linked polyhexopyranoses (hexopyranans). Recently, Kobayashi et al. reported that (1→4)-β-D-glucopyranan, i.e., cellulose, was synthesized by the enzymatic polymerization of β-cellubiosyl fluoride (Scheme 1.4).[23,24]

Scheme 1.4



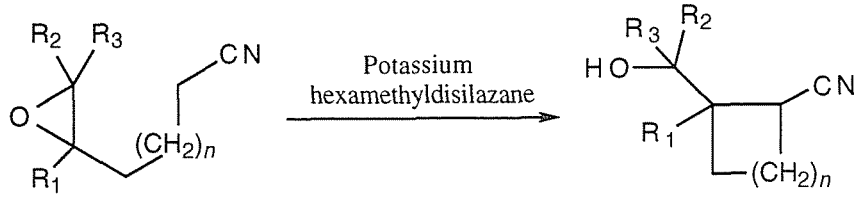
1.2 Cyclopolymerization aiming to synthesize polysaccharide

1.2.1 Ring-opening and Cyclization of Epoxides

Optically active epoxides are widely used as a chiral building block for the syntheses of naturally occurring compounds and many other well-stereocontrolled products. For these syntheses, the chiral epoxide needs to react

regio- and stereoselectively with the appropriate substrates. The regio- and stereoselective synthesis of chiral compounds using cyanoepoxides, hydroxyepoxides and diepoxides is a particularly useful synthetic strategy.[25-32] Stork et al. drew the conclusion that the cyclization of cyanoepoxide always yields the smaller ring in preference to the larger ring. This is true when the ring formed is three-, four-, five-, and six-membered (Scheme 1.5).[25]

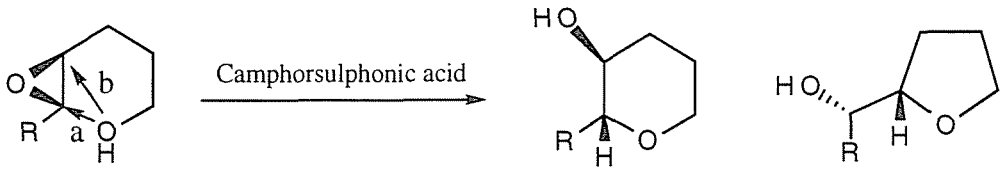
Scheme 1.5



n=0,1,2,3

Nicolaou et al. reported a stereospecific route to synthesize tetrahydropyrans and tetrahydrofurans from 5-substituted-4,5-epoxy-1-ol via the 6-endo and the 5-exo mode of epoxide opening, respectively (Scheme 1.6).[26,27]

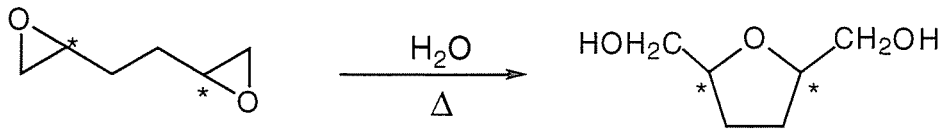
Scheme 1.6



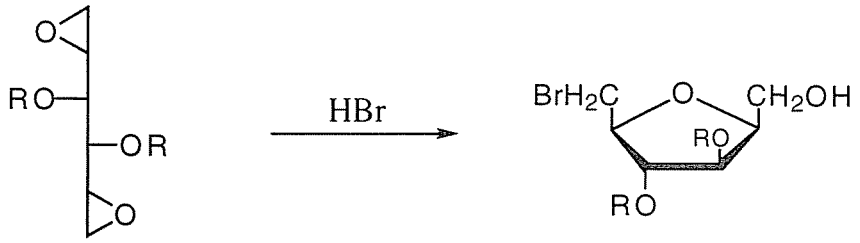
a: 6-endo b: 5-exo

Wiggins and Wood reported that 1,2:5,6-diepoxyhexane reacted with water to form the corresponding 2,5-bis(hydromethyl)tetrahydrofuran.[28] Similarly, Kuszmann reported that the regio- and stereoselective cyclizations of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol and -L-iditol with hydrogen bromide produced the corresponding 2,5-anhydro-6-bromo-6-deoxy-D-glucitol and 2,5-anhydro-1-bromo-1-deoxy-D-glucitol, respectively (Scheme 1.7).[29]

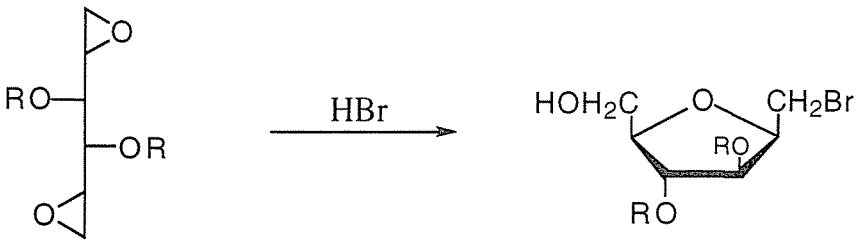
Scheme 1.7



1,2:5,6-Diepoxyhexane



1,2:5,6-Dianhydro-
D-mannitols



1,2:5,6-Dianhydro-
L-iditols

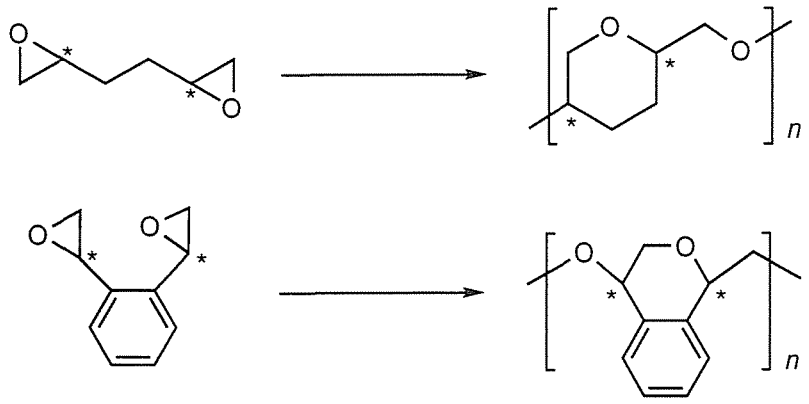
The cyclization of the diepoxide, in particular, 1,2:5,6-dianhydrohexitol, is an interesting subject in terms of the regio- and stereoselectivity of the resulting products.

1.2.2 Cyclopolymerization of Diepoxides

Several reports were published on the cyclopolymerization of diepoxides such as 1,2-bis(epoxyethyl)benzene, 1,2:5,6-diepoxyhexane, *N*,*N*-bis(2,3-epoxypropyl)aniline, and 1,2-bis[2-(2,3-epoxypropoxy)ethoxy]-benzene.[33-37] The cyclopolymerization of the diepoxide is a facile method to synthesize polymers with ether linkages and characteristic cyclic units in the main chain.

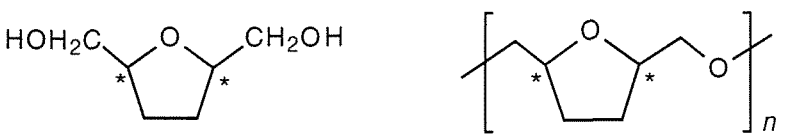
Stille et al. reported that the cyclopolymerization of the enantiomeric and diastereomeric mixtures of 1,2:5,6-diepoxyhexane by cationic and heterogeneous anionic catalysts produced the soluble polymer without residual epoxy groups.[33,34] The soluble polymer consisted of enchained tetrahydropyran units through an intramolecular-intermolecular propagation mechanism. Aso et al. also reported a similar result for the cyclopolymerization of 1,2-bis(epoxyethyl)benzene which corresponds to a benzene derivative of 1,2:5,6-diepoxyhexane (Scheme 1.8).[35]

Scheme 1.8



On the other hand, Bauer reported that the cyclopolymerization of 1,2:5,6-diepoxyhexane using soluble anionic catalysts yielded the linear polymers consisting of symmetrically substituted tetrahydrofuran rings.[36] The conclusion was drawn from the comparison of the IR and ^{1}H NMR spectra between the polymer and the cyclic model compound obtained by hydrolysis of the diepoxides (Chart 1.1).

Chart 1.1

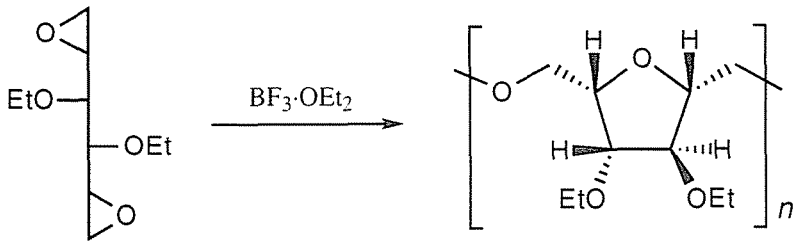


The cyclopolymerization of the 1,2:5,6-diepoxyhexanes, therefore, produced soluble polymers consisting of tetrahydropyran or tetrahydrofuran units depending on the catalyst used. However, the cyclic constitutional units of the polymer were stereoisomeric mixtures. The stereoselective synthesis of the polymer is greatly to be desired.

1,2:5,6-Dianhydrohexitol, which corresponds to the 3,4-dihydroxy substituted 1,2:5,6-diepoxyhexane, have definite absolute configurations at four asymmetric carbon atoms. The dianhydrohexitol, therefore, is very useful diepoxide to discuss the cyclopolymerization tendency and the stereochemistry of polymerization. The cyclopolymerization of the diepoxide presents a new preparative method for synthetic polysaccharide.

Recently, Hashimoto et al. reported that 1,2:5,6-dianhydro-3,4-di-*O*-ethyl-D-mannitol was cyclopolymerized with cationic catalyst to form the polymer mainly consisting of 2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol as the cyclic constitutional repeating unit, as shown in Scheme 1.9.[38]

Scheme 1.9



1.3 Object and Outline of the Thesis

There is a distinct difference not only in mode of polymerization, but also in structure of polymer between the cyclopolymerization of dianhydrosugar and the ring-opening polymerization of anhydrosugar for synthesizing polysaccharide. The polymer obtained from the cyclopolymerization of 1,2:5,6-dianhydrohexitol is a new type of

polysaccharides which lacks the anomeric linkage. Therefore, it is important to elucidate the cyclopolymerization tendency of the dianhydrosugar and to characterize the structure of the resulting polymer. The present study focuses on the cyclopolymerization of 1,2:5,6-dianhydrohexitol.

The objects of this study are to clarify the polymerization character and the stereochemical factor on the cyclopolymerization of 1,2:5,6-dianhydrohexitol and to establish a new synthetic method of polysaccharide.

The outline of this thesis is as follows:

In Chapter 2, the polymerization tendency of 1,2:5,6-dianhydro-D-mannitols and their substituent effects in the 3,4-*O*-positions are studied on the cationic cyclopolymerization. The polymerization proceeded regio- and stereoselectively to produce the polymer consisting of 2,5-anhydro-D-glucitol as most of the cyclic constitutional unit and 2,6-anhydro-D-glucitol as least of the unit.

Chapter 3 describes the cyclopolymerization of 1,2:5,6-dianhydro-D-mannitols using anionic initiator. The regio- and stereoselectivity of the cyclopolymerization is discussed by comparing the spectral characteristics of the resulting polymers with those of the cyclic model compounds. The anionic cyclopolymerization was more regio- and stereoselective than that using cationic catalysts and produced a well-defined polymer, that is, (1→6)-3,4-di-*O*-alkyl-2,5-anhydro-D-glucitol, which has a hydroxymethyl and a *tert*-butoxy group at each of the chain ends.

In Chapter 4, the cyclopolymerizations of (2*S*,5*S*)-1,2:5,6-diepoxyhexane, which corresponds to the 3,4-substituent-free compound of 1,2:5,6-dianhydro-D-mannitols, using cationic and anionic initiators are reported. For the polymer obtained using cationic catalyst, the constitutional repeating units were the 5- and 6-membered rings together with a pendant epoxy group unit. The polymer using anionic catalyst essentially consisted of

polysaccharides which lacks the anomeric linkage. Therefore, it is important to elucidate the cyclopolymerization tendency of the dianhydrosugar and to characterize the structure of the resulting polymer. The present study focuses on the cyclopolymerization of 1,2:5,6-dianhydrohexitol.

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the 5-membered cyclic repeating unit.

Chapter 5 describes the cationic and anionic cyclopolymerizations of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-L-iditol, which is a diastereomer of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol, in order to obtain further information on the regio- and stereoselective cyclopolymerizations of 1,2:5,6-dianhydrohexitols. The configurational relationship between the homopolymers obtained from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-L-iditol and 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol was also discussed on the basis of the copolymerization between these monomers.

Chapter 6 reports the cyclopolymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-glucitol using cationic and anionic catalysts. The polymerizations proceeded through the cyclopolymerization mechanism leading to polymers with cyclic constitutional units. The cationic cyclopolymerization yielded the polymer consisting mainly of 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol units. The anionic polymerization involved two processes to yield the polymer consisting of 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol and L-iditol units.

Finally, Chapter 7 summarizes the results in this study.

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Chapter 2

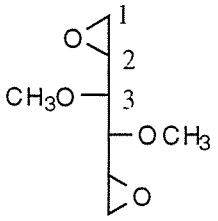
Cationic Cyclopolymerization of 1,2:5,6-Dianhydro-3,4-di-*O*-alkyl-D-mannitols to Form (1→6)-2,5-Anhydro-3,4-di-*O*-alkyl-D-glucitols

2.1 Introduction

Recently, Hashimoto et al. reported that 1,2:5,6-dianhydro-3,4-di-*O*-ethyl-D-mannitol was polymerized using BF_3•OEt_2 to form a gel-free polymer.[1] The polymerization proceeded through a cyclopolymerization mechanism and the resulting polymer mainly consisted of five-membered unit.

The object in this chapter is to explore the character of the cyclopolymerization which has a possibility for a new synthetic method of artificial polysaccharides. Substituent effects in the 3,4-positions of 1,2:5,6-dianhydro-D-mannitols, namely, 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**), 3,4-di-*O*-ethyl-D-mannitol (**2**), 3,4-*O*-isopropylidene-D-mannitol (**3**), 3,4-di-*O*-pentyl-D-mannitol (**4**), and 3,4-di-*O*-decyl-D-mannitol (**5**) are

Chart 2.1



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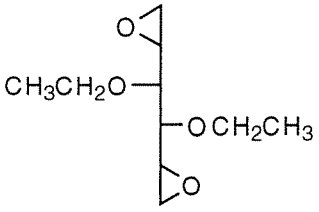

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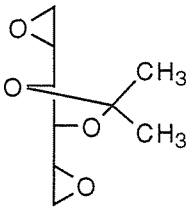

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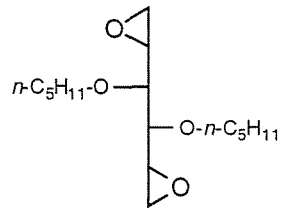
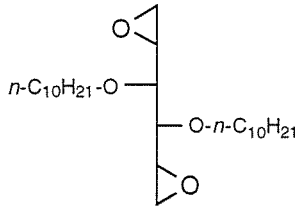


4



5

studied on the cationic polymerization. Monomers **1** and **2** present the basic character of the regio- and stereoselectivity on the polymerization. Monomer **3** is used for clarifying the substituent effect on the cyclopolymerization tendency. Monomer **4** and **5** lead to a more extensive investigation into the adaptability of the polymerization.

2.2 Results

2.2.1 Monomer preparation

Monomers **1**, **2** and **4** were prepared from D-mannitol according to the reported procedure.[2] The monomers are colorless liquid at room temperature. For monomer **1**, total carbons are eight, but only four peaks are formed in the ^{13}C NMR spectrum as shown in Figure 2.1. The fact is caused by the C_2 symmetric character of the monomer. The ^{13}C NMR spectra of **2** and **4** also reveal that the compounds have a C_2 symmetry.

Monomer **5** was synthesized using the procedure similar to that for **4**, as shown in Scheme 2.1. On the other hand, the method of Merrer et al. was used to synthesize monomer **3**.[3] Since the monomer is substituted with

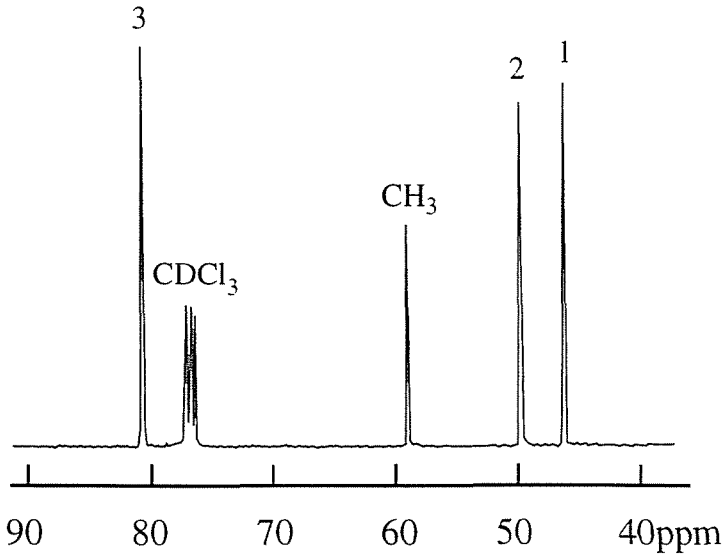
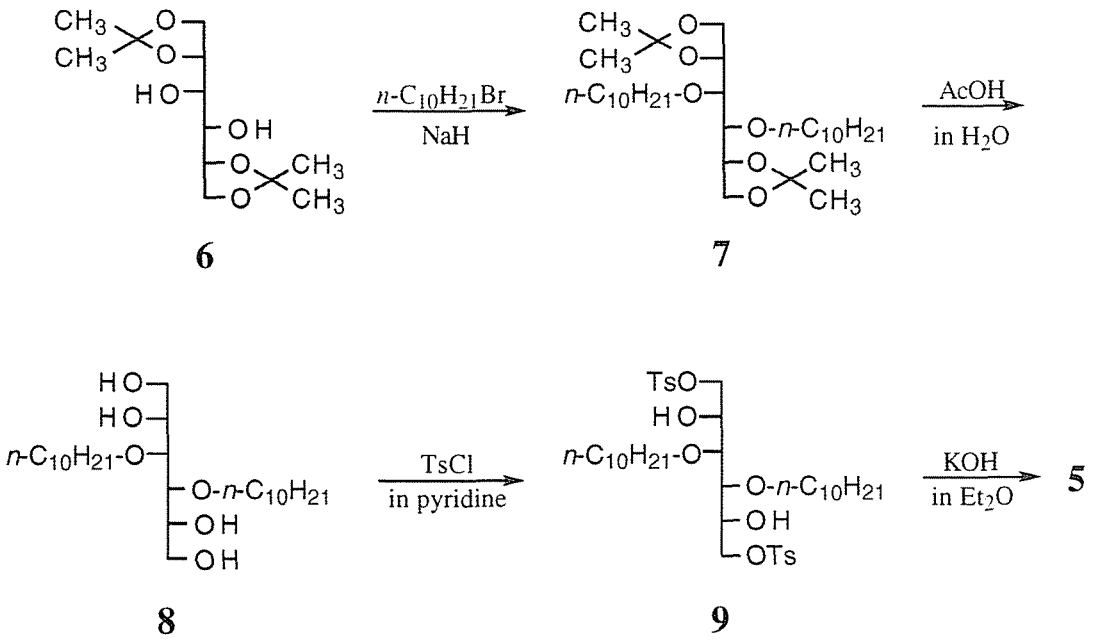


Figure 2.1. ^{13}C NMR spectrum of 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**).

isopropylidene group at 3,4-positions, the bond between the carbons at 3,4-positions can not rotate freely. Monomers **3** and **5** are also C_2 symmetrical compounds.

Scheme 2.1



2.2.2 Polymerization of 1,2:5,6-dianhydro-3,4-di-O-methyl-D-mannitol

Table 2.1 summarizes the results of the polymerization of monomer **1**. For the polymerization with $BF_3 \cdot OEt_2$, the reaction systems were homogeneous except the case used toluene as a solvent. The products obtained were sticky, semi-solid which were soluble in chloroform, tetrahydrofuran, methanol, and water, but insoluble in *n*-hexane. For the polymerization in dichloromethane at -30 °C, the highest polymer yield attained to 68.3 %. The polymerization in toluene at 0°C proceeded heterogeneously, and the organic solvent-soluble polymer was obtained in 51.9 % yield together with the organic solvent-insoluble one in 14.6 % yield. After the polymerization for 24 h, the monomer was recovered in a small amount at -30 °C, though completely consumed at 0 °C. The low molecular weight products as *n*-hexane-soluble part were obtained by separating insoluble polymers from the raw products. The *n*-hexane-insoluble

polymers obtained at -30 °C had the number-average molecular weights (M_n) of 1010~1490 which corresponded to the average degree of polymerization (DP_n) of 5.8~8.6, but those at 0 °C increased the M_n to 1450~3370 corresponding to DP_n of 8.3~19.4 on the basis of polystyrene standards by means of a gel permeation chromatography (GPC) in THF. The further polymerization did not cause to increase the yield and M_n of the polymers, resulting from the end of polymerization within about 24 h.

For the polymerizations with $SnCl_4$ for 24 h, the polymers were obtained in very low yields and most of the monomer was recovered. The polymers were sticky, semi-solid with the M_ns of 1700 and 2500. The $SnCl_4$ catalyst was less effective than the $BF_3 \cdot OEt_2$ catalyst for the polymerization.

The specific rotations ($[\alpha]^{22}_{546}$) of the polymers changed in the range of +41.3°~+73.2° (*c* 1.0 in $CHCl_3$). An obvious relation between the specific rotation and the M_n, however, was not found and thus the origin of the change was obscure.

Table 2.1. Cationic polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (1)[a]

Catalyst	Solvent	Temp °C	Yield %	M_n[b]	M_w/M_n[b]	DP_n	$[\alpha]^{22}_{546}$[c]
$BF_3 \cdot OEt_2$	$C_6H_5CH_3$	-30	12.5	1010	1.77	5.8	+64.5
	$ClCH_2CH_2Cl$	-30	42.7	1490	2.68	8.6	+62.6
	CH_2Cl_2	-30	68.3	1300	2.51	7.5	+70.4
	$C_2H_5NO_2$	-30	28.1	1080	1.94	6.2	+71.3
	$C_6H_5CH_3$	0	51.9[d]	3370	2.38	19.4	+63.5
	CH_2Cl_2	0	48.9	2650	2.03	15.2	+41.3
	CH_2Cl_2[e]	0	48.3	2480	1.89	14.4	+43.0
	$C_6H_5NO_2$	0	40.5	1450	2.33	8.3	+73.2
	$C_2H_5NO_2$	0	51.4	1730	1.73	9.9	+52.9
$SnCl_4$	CH_2Cl_2	-30	trace	1700	1.66	9.8	+59.2
	CH_2Cl_2	0	7.9	2500	2.26	14.4	+46.2

[a] [**1**]=0.5 mol•L^{-1}; [**1**]/[Catalyst]=100; time, 24h. [b] Measured in THF by GPC using PSt as standard. [c] Measured in $CHCl_3$ (*c* 1.0). [d] Organic solvent-insoluble polymer was 14.6%. [e] Time, 2h.

2.2.3 *Polymerization of 1,2:5,6-dianhydro-3,4-di-O-ethyl-D-mannitol and -3,4-O-isopropylidene-D-mannitol*

The cationic polymerizations of monomers **2** and **3** were carried out with $BF_3 \cdot OEt_2$ and $SnCl_4$ in dichloromethane, nitroethane, and toluene. Table 2.2 lists the polymerization results of **2**. The $SnCl_4$ catalyst was inactive in the polymerization and most of the monomer was recovered after polymerization for 24 h. On the other hand, the polymerization by the $BF_3 \cdot OEt_2$ catalyst proceed homogeneously. Although all the monomer was consumed, a small amount of the *n*-hexane-insoluble polymer (20~35 % yield) was formed concurrently with a considerable amount of *n*-hexane-soluble low molecular weight products. The polymers were sticky semi-solids, and soluble in chloroform, tetrahydrofuran, methanol, and water except that the polymer obtained in toluene contained a small portion of the organic solvent-insoluble part. The M_n of the polymer was 4900 for the polymerization in toluene, 6140 in dichloromethane, and 2780 in nitroethane, corresponding to the DP_n in the range of 14 to 30. The $[\alpha]^{22}_{546}$ of the polymer obtained was +42.7°~54.3° (*c* 1.0 in $CHCl_3$).

Table 2.2. Cationic polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-ethyl-D-mannnitol (2)[a]

Catalyst	Solvent	Yield[b] %	M_n[c]	M_w/M_n[c]	DP_n	$[\alpha]^{22}_{546}$[d]
$BF_3 \cdot OEt_2$	$C_6H_5CH_3$	34.3[e]	4900	1.90	24.3	+49.8
$BF_3 \cdot OEt_2$	CH_2Cl_2	20.7	6140	1.66	30.4	+42.7
$BF_3 \cdot OEt_2$	$C_2H_5NO_2$	22.3	2780	1.52	13.8	+54.3
$SnCl_4$	$C_6H_5CH_3$	trace	-			
$SnCl_4$	CH_2Cl_2	trace	-			
$SnCl_4$	$C_2H_5NO_2$	trace	-			

[a] [**2**]=0.5 mol•L^{-1}; [**2**]/[Catalyst]=100; time, 24h; temp, 0℃. [b] Yields of $CHCl_3$-soluble polymer. [c] Measured in THF by GPC using PSt as standard. [d] *c* 1.0, chloroform. [e] Organic solvent-insoluble polymer was 8.2%.

Monomer **3**, which exhibits hindered rotation of the C-C bond between 3- and 4-positions, was compared the cyclopolymerization tendency with monomers **1** and **2**. Table 2.3 lists the results of the polymerization of **3**. The polymerization proceeded with $BF_3 \cdot OEt_2$ and $SnCl_4$ to form powdery polymers which were soluble in chloroform, tetrahydrofuran, and methanol, but insoluble in *n*-hexane. The polymer obtained using $BF_3 \cdot OEt_2$ in toluene contained a small portion of the organic solvent-insoluble part. Much more yields, but lower M_ns were given the polymers with the $BF_3 \cdot OEt_2$ catalyst in comparison with the $SnCl_4$ catalyst. The values of $[\alpha]^{22}_{546}$ varied from +7.6° to +14.5° (*c* 1.0 in $CHCl_3$).

The polymerization with $BF_3 \cdot OEt_2$ gave higher M_ns the polymers from monomer **1** and **2** than the polymer from monomer **3**, but that with $SnCl_4$ the opposite result. Toluene and dichloromethane as a polymerization solvent were more effective in the M_ns of the polymers than nitroethane.

Table 2.3. Cationic polymerization of 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol (3)[a]

Catalyst	Solvent	Yield[b] %	M_n[c]	M_w/M_n[c]	DP_n	f_c[d]	$[\alpha]^{22}_{546}$[e]
$BF_3 \cdot OEt_2$	$C_6H_5CH_3$	20.4[f]	2,510	2.21	13.5	0.58	+14.5
$BF_3 \cdot OEt_2$	CH_2Cl_2	39.5	2,000	1.63	10.8	0.56	+7.6
$BF_3 \cdot OEt_2$	$C_2H_5NO_2$	20.6	1,090	1.25	5.9	0.45	+8.8
$SnCl_4$	$C_6H_5CH_3$	12.6	3,830	2.30	20.6	0.46	+11.8
$SnCl_4$	CH_2Cl_2	13.3	3,040	1.71	16.3	0.53	+9.9
$SnCl_4$	$C_2H_5NO_2$	9.6	1,750	1.77	9.4	0.57	+11.1

[a] [**3**]=0.5 mol•L^{-1}; [**3**]/[Catalyst]=100; time, 24h; temp, 0℃. [b] Yields of $CHCl_3$-soluble polymer. [c] Measured in THF by GPC using PSt as standard. [d] Mole fraction of the cyclic structure units in the polymer. [e] *c* 1.0, chloroform. [f] Organic solvent-insoluble polymer was 12.4%.

2.2.4 Polymerization of 1,2:5,6-dianhydro-3,4-di-O-pentyl-D-mannitol and -3,4-di-O-decyl-D-mannitol

Table 2.4 lists the results of the polymerizations of **4** and **5** using BF_3•OEt_2. All the polymerization proceeded homogeneously. After 24 h at 0 °C, the reaction mixture was poured into methanol containing a drop of aqueous ammonia and the solution was evaporated to yield an oil residue consisting of the monomer and polymer. Monomer **4** could not be removed from the polymers by the usual reprecipitation method, because the monomer resembles the polymers in solubility to *n*-hexane, $CHCl_3$, THF, and MeOH. A small difference in solubility to *n*-hexane and MeOH between the monomer and the polymer was used for separating both parts. The mixture was extracted using *n*-hexane/MeOH, and the MeOH layer was evaporated under reduced pressure. This procedure was repeated until the absence of the monomer was confirmed in MeOH phase using GPC measurement. For the polymerization in CH_2Cl_2, the yield was 31.6 % and the M_n was 6200 which corresponded to a DP_n of 21.6. However the purification of the raw products obtained in $C_6H_5CH_3$ and $C_2H_5NO_2$ was incomplete because of their lower M_ns. The values of 2700 and 2600 listed in Table 2.4 were estimated from the GPC traces of the mixtures. On the other hand, the polymers from **5** were soluble in *n*-hexane, $CHCl_3$, and THF but insoluble in MeOH, so that they were purified by reprecipitation from *n*-hexane/MeOH. The polymer yields were 44.5~48.9 % and the M_ns were 3900~4600 (DP_n = 9.1~10.8). The specific rotation ($[\alpha]^{22}_D$) was +25.8° for the polymer from **4** and +14.4°~+16.0° for those from **5** (*c* 1.0 in $CHCl_3$).

The polymers synthesized from **4** and **5** were soluble in common organic solvents but insoluble in MeOH and water, which differed from polymer from **1~3** in to be not amphiphilic. The polymers prepared in $C_2H_5NO_2$ had lower M_ns than those in CH_2Cl_2 expect for the case of monomer **5**. The polymerizations of **1~3** in toluene proceeded heterogeneously. The polymerizabilities of the monomers depended on the character of substituents in

3,4-positions and increased in the order of **2**>**4**>**1**>**5**≥**3**.

Table 2.4. Cationic polymerization of 1,2:3,4-dianhydro-3,4-di-*O*-pentyl-D-mannitol (4) and 1,2:3,4-dianhydro-3,4-di-*O*-decyl-D-mannitol (5)[a]

Monomer	Solvent	Temp.	Yield (%)	M_n	M_w/M_n[b]	DP_n	$[\alpha]^{22}_{546}$[c]
4	$C_6H_5CH_3$	0°C	-	2700	1.22	9.4	-
	CH_2Cl_2	0°C	31.6	6200	1.34	21.6	+25.8
	$C_2H_5NO_2$	0°C	-	2600	1.61	9.1	-
5	$C_6H_5CH_3$	0°C	44.5	4180	1.20	9.8	+15.6
	CH_2Cl_2	-30°C	21.8	3130	1.44	7.3	+14.8
	CH_2Cl_2	-5°C	28.4	3430	1.45	8.0	+14.3
	CH_2Cl_2	0°C	46.2	3920	1.41	9.2	+16.0
	CH_2Cl_2	5°C	42.6	3180	1.36	7.5	+14.5
	$C_2H_5NO_2$	0°C	48.9	4580	1.29	10.7	+14.4

[a] Catalyst, $BF_3 \cdot OEt_2$; [Monomer] = 0.5 mol•L^{-1}; [Monomer]/[$BF_3 \cdot OEt_2$] = 100; temp, 0 ℃; time, 24 h. [b] Estimated by GPC using polystyrene as standard. [c] *c* 1.0 in $CHCl_3$.

2.3 Discussion

2.3.1 Polymer structure

Figure 2.2(a) shows the ^{1}H NMR spectrum of the polymer obtained from **1**. Since the characteristic signals at 3.1~3.2 and 2.7~3.0 ppm due to the epoxy groups completely disappeared, the polymerization proceeded according to a cyclopolymerization mechanism leading to the polymer with cyclic constitutional repeating units, i.e., the mole fraction of the cyclic structural units (f_c) was 1.0.

The polymerizations of monomers **2**, **4** and **5** similarly proceeded according to the cyclopolymerization mechanism, because the ^{1}H NMR spectra of the polymers indicated the absence of the epoxy group. On the other hand, the ^{1}H NMR spectrum of the polymer from **3** showed the characteristic resonances at δ=2.6~3.2 ppm due to the methylene and the methine protons of

the epoxide (Figure 2.2(b)). The f_cs of the resulting polymers were 0.45~0.58, which were determined from the relative peak areas of the protons at 2.6~3.0 and 1.1~1.7 ppm in the ^{1}H NMR spectra. This indicates that the polymerization of **3** is difficult to induce intramolecular cyclization, because of the prohibition of rotation at 3,4-positions.

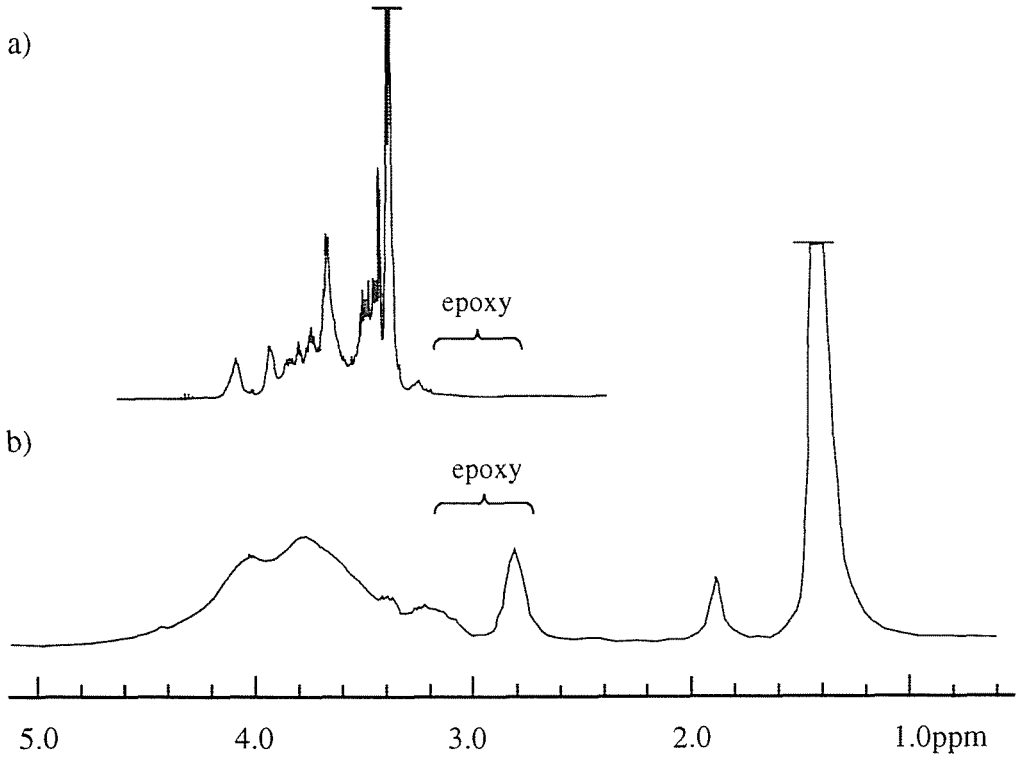
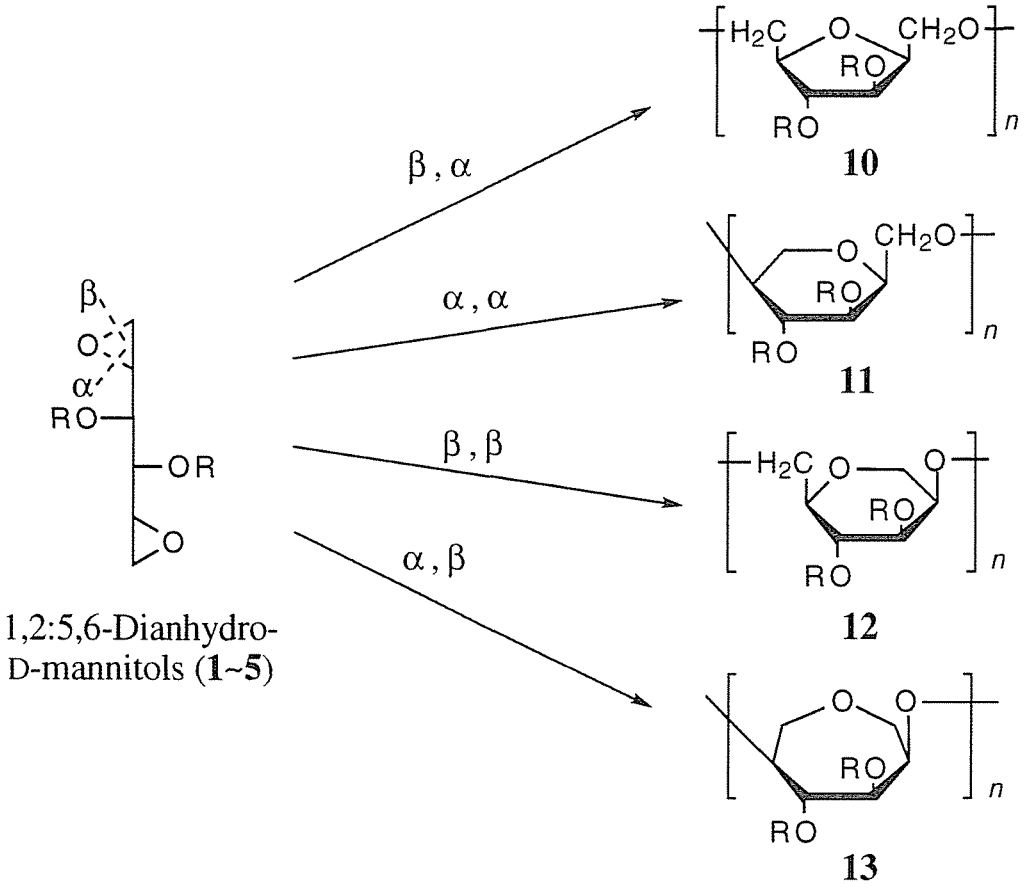


Figure 2.2. ^{1}H NMR spectra of the polymers obtained from (a) 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) and (b) 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol (**3**) using BF_3•OEt_2.

For the cationic polymerization of monosubstituted epoxides through an S_N2-type mechanism, the configuration of the asymmetric carbon atom is inverted due to the ring-opening at the CH-O bond (α-scission), and retained by the CH_2-O bond (β-scission).[4] For the cyclopolymerization of the enantiomeric and the diastereomeric mixtures of diepoxides, there are many possible cyclic repeating units. For the cyclopolymerization of **1~5**, however, the number of possible cyclic units in the polymer are only four because monomers **1~5** have the C_2 symmetrical properties. Scheme 2.2 represents the possible cyclic units

formed through the S_N2-type mechanism. When the intermolecular reaction and the intramolecular cyclization proceed through β,α- and α,β-scissions of the two epoxides in a monomer molecule, the structure of cyclic unit consist of the 5- and 7-membered rings **10** and **13**, respectively. On the other hand, α,α- and β,β-scissions lead to the formation of the 6-membered rings **11** and **12**, respectively.

Scheme 2.2.[a]

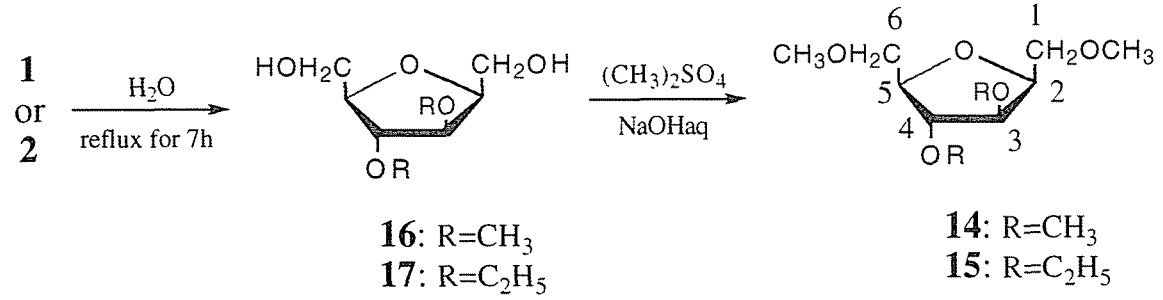


[a] The former and latter symbols correspond to the intermolecular and intramolecular scissions, respectively

In order to confirm the cyclic units in the polymers from **1** and **2**, 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol (**14**) and 2,5-anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol (**15**) were synthesized from **1** and **2** using the procedure similar to that of Wiggins et al.[5]; the products by the hydrolysis of

1 and **2** are 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol (**16**) and 2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol (**17**), respectively, and then these compounds are treated with dimethyl sulfate to yield the model compounds **14** and **15** (Scheme 2.3).

Scheme 2.3



16: R=CH_3
17: R=C_2H_5

14: R=CH_3
15: R=C_2H_5

Figure 2.3 shows the ^{13}C NMR spectra of **14** and the polymer from **1**. Each of the signals was assigned as follows: for **14**, the signals at 85.69 (C3), 84.75 (C4), 82.26 (C2) and 79.83 (C5) ppm were the methine carbons and those at 73.15 (C1) and 70.66 (C6) ppm, the methylene ones, and for the polymer from **1**, the signals at 85.41, 84.68, 82.27 and 79.86 ppm were the methine carbons and those at 71.72 and 69.32 ppm, the methylene ones. The four signals due to the methine carbons for the polymer are very close to those for **14**. This result indicates that the structure of the polymers from **1** is (1→6) bonded 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol as the 5-membered constitutional unit (i.e., **10** in Scheme 2.2).

The ^{13}C NMR spectra of **15** and the polymer from **2** are shown in Figure 2.4. The signals at 84.32, 83.13, 82.44, and 79.84 ppm for the polymer are close to the carbons of C3, C4, C2, and C5, respectively, for **15**. Therefore, the polymer from **2** also contains the (1→6)-linked 2,5-anhydro-D-glucitol unit (Scheme 2.4).

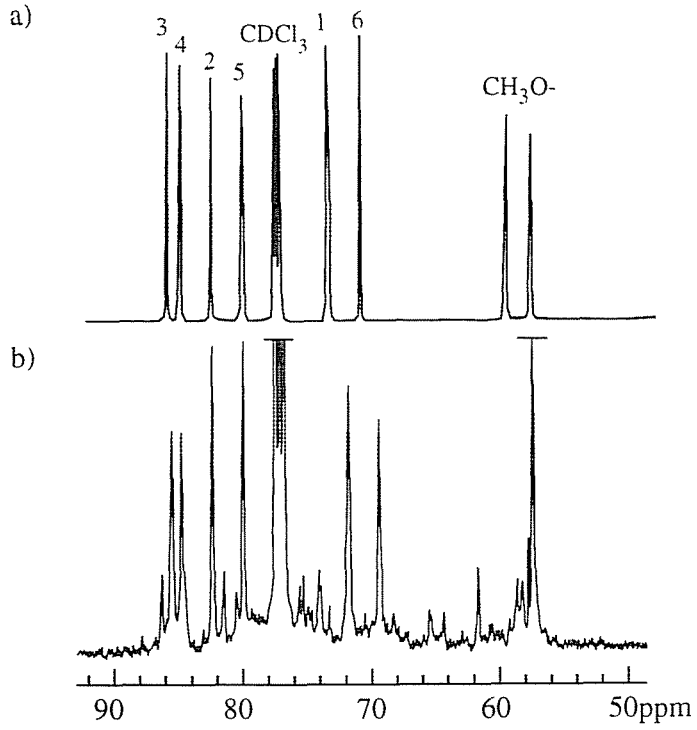


Figure 2.3. ^{13}C NMR spectra of (a) 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol (**14**) and (b) the polymer prepared from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) using $BF_3 \cdot OEt_2$.

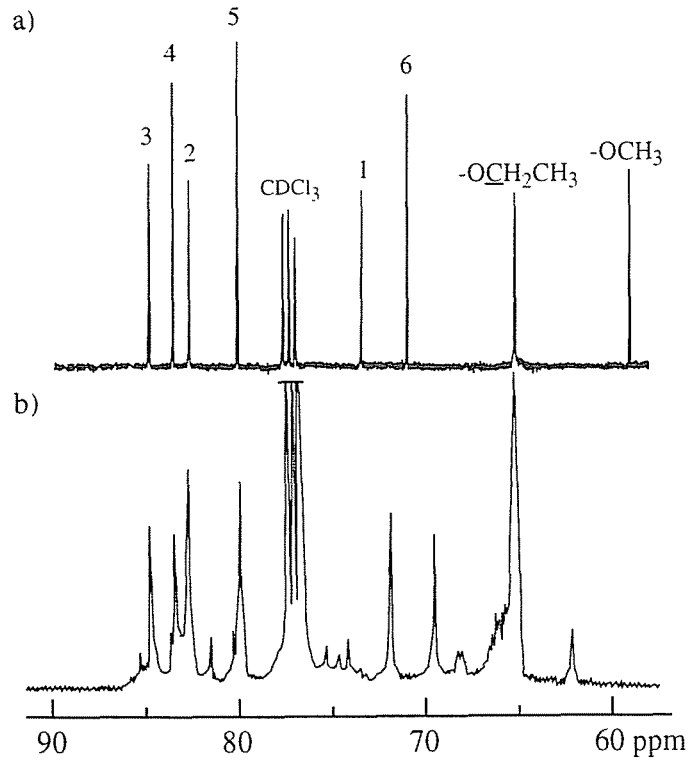


Figure 2.4. ^{13}C NMR spectra of (a) 2,5-anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol (**15**) and (b) the polymer obtained from 1,2:5,6-dianhydro-3,4-di-*O*-ethyl-D-mannitol (**2**) using $BF_3 \cdot OEt_2$.

The ^{13}C NMR spectra of the polymers obtained from **4** and **5** using $BF_3 \cdot OEt_2$ are shown in Figure 2.5. For the polymer from **4**, the signals at 84.38, 83.26, 82.44 and 79.97 ppm were the methine carbons and those at 71.96 and 69.39 ppm were the methylene ones, and for the polymer from **5**, those at 84.45, 83.25, 82.38 and 79.92 ppm were the methine carbons and those at 72.00 and 69.30 ppm were the methylene ones. Both of the four signals due to the methine carbons are very close to those for the carbons of C3, C4, C2, and C5 of the polymer from **2**, respectively. This result indicates that the structures of the polymers from both **4** and **5** were also the (1→6) bonded 2,5-anhydro-D-mannitol unit (Scheme 2.4).

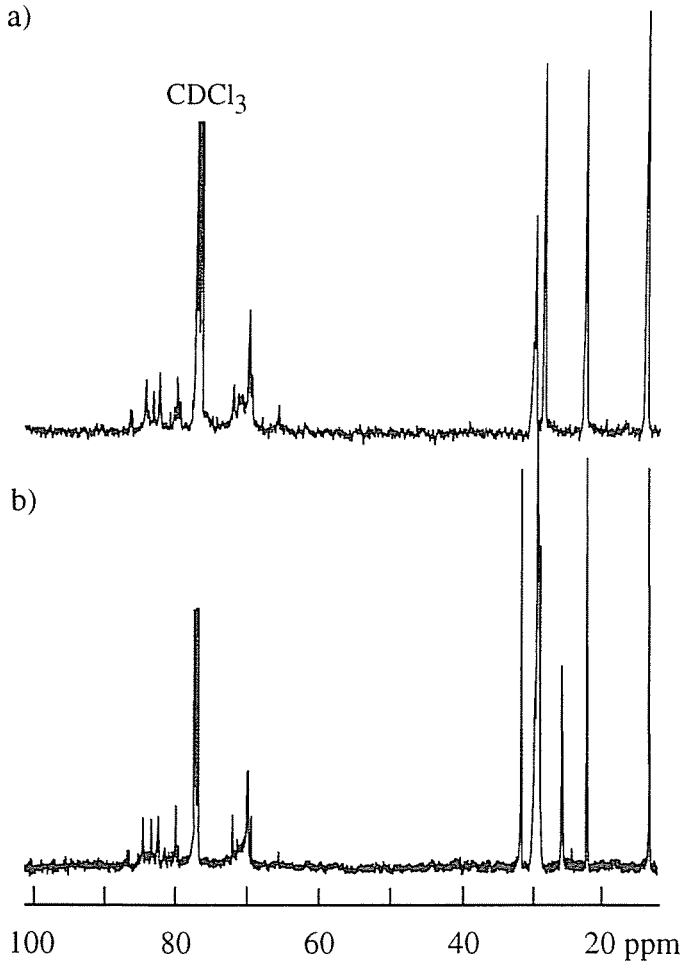
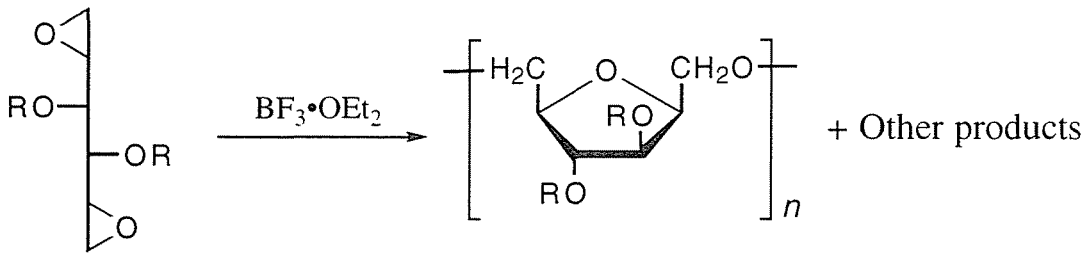


Figure 2.5. ^{13}C NMR sprctra of the polymers prepared from (a) 1,2:5,6-dianhydro-3,4-di-*O*-pentyl-D-mannitol (**4**) and (b) 1,2:5,6-dianhydro-3,4-di-*O*-decyl-D-mannitol (**5**) using $BF_3 \cdot OEt_2$.

Scheme 2.4



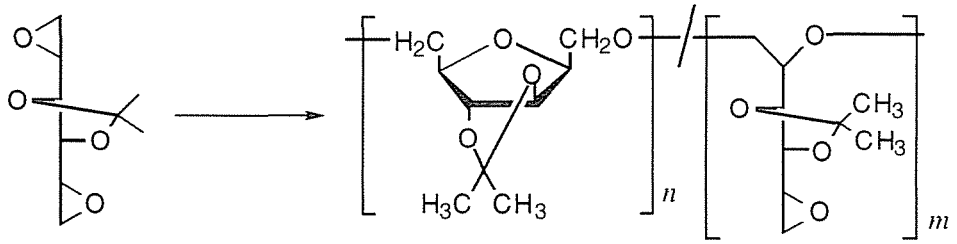
1: R= CH_3
2: R= C_2H_5
4: R= *n*-C_5H_{11}
5: R= *n*-$C_{10}H_{21}$

10a: R= CH_3
10b: R= C_2H_5
10c: R= *n*-C_5H_{11}
10d: R= *n*-$C_{10}H_{21}$

However, several minor signals were observed in the ^{13}C NMR spectra of polymers obtained from **1**, **2**, **4** and **5**. The polymer, thus, should contain a slight amount of other cyclic repeating units, except for 2,5-anhydro-D-mannitol unit. The further discussion must await the syntheses of other possible cyclic units of **11**, **12**, and **13**.

Wiggins reported that the hydrolysis of **3** formed none of cyclic compounds under the same condition in which **1** was refluxed in water to yield cyclic unimer **16**.[5] The lower cyclization tendency of **3** should be caused by the prohibition of the free rotation around the C3 and C4 linked with the *O*-isopropyridene group, thus diminishing the ability in the intramolecular cyclization. The polymerizations of **3** with BF_3•OEt_2 and $SnCl_4$ produced polymers **10e** with cyclic and acyclic units. The extent of cyclization was about

Scheme 2.5



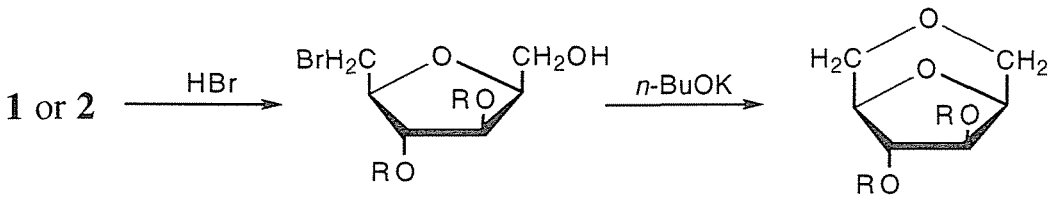
3 **10e**

0.5. The proposed structure of the resulting polymers is shown in Scheme 2.5. The structure of the cyclic unit in polymer **10e** should mainly consist of a five-membered unit.

2.3.2 Oligomer structure

Isolation of the *n*-hexane-soluble oligomer was carried out by fractional precipitation of the raw product obtained from the polymerization of **1** using BF_3•OEt_2. After purification by preparative thin layer chromatography, a clear compound with *m/z*= 174 and $[\alpha]^{22}_{546}$ = -22.8° (*c* 1.0, $CHCl_3$) was isolated in 30 % yields. On the other hand, for the polymerization of **2**, a compound with *m/z*= 202 and $[\alpha]^{22}_{546}$= -37.5° (*c* 1.0, $CDCl_3$) was isolated in 65.3 % yield. These isolated products were confirmed to be 1,6:2,5-dianhydro-3,4-di-*O*-methyl-D-glucitol (**19**) and 1,6:2,5-dianhydro-3,4-di-*O*-ethyl-D-glucitol (**21**) by direct comparison with authentic samples prepared independently (Scheme 2.6).

Scheme 2.6

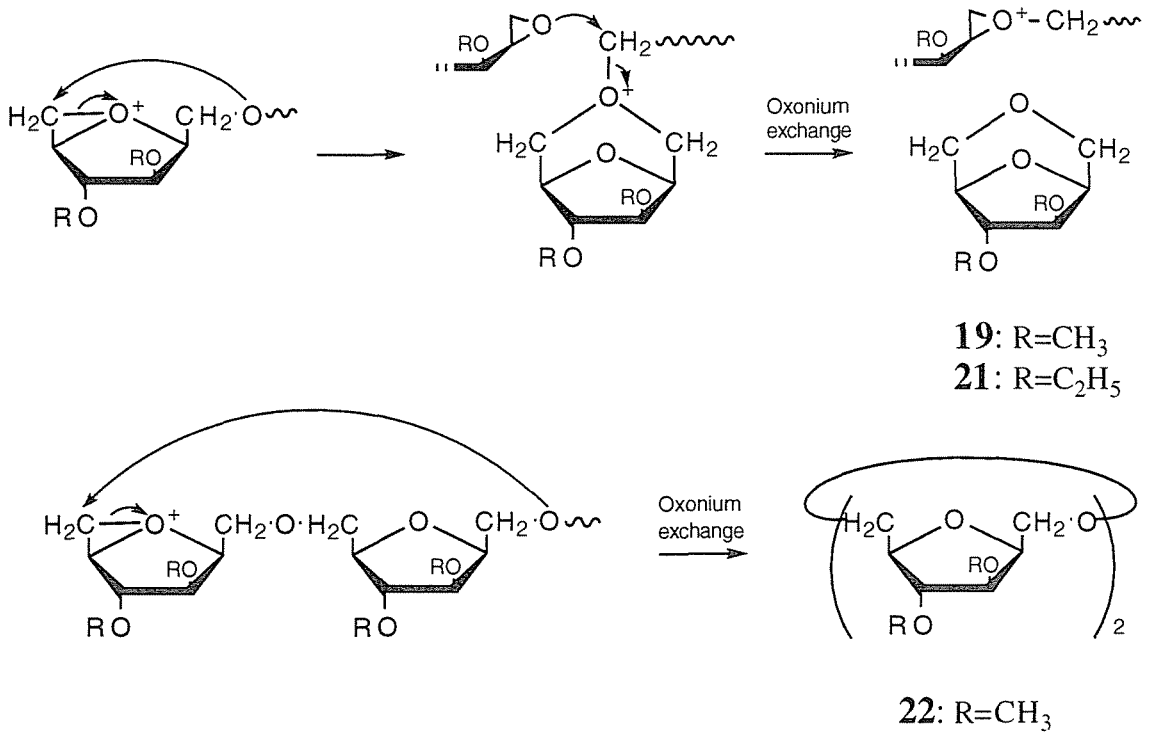


18: R=CH_3
20: R=C_2H_5

19: R=CH_3
21: R=C_2H_5

In addition, the compound with *m/z*= 348 was obtained in 6 % yield for **1**, which was estimated to be a cyclic dimer (**22**) of 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol. In the mass spectrum, the presence of the cyclic trimer, tetramer, and pentamer being the higher homologies of **22** was detected. The formation of these oligomers should be caused by unimolecular bicyclic reaction of the diepoxide with cationic species and/or by back-biting of the growing chain end through oxonium cation exchange (Scheme 2.7).

Scheme 2.7



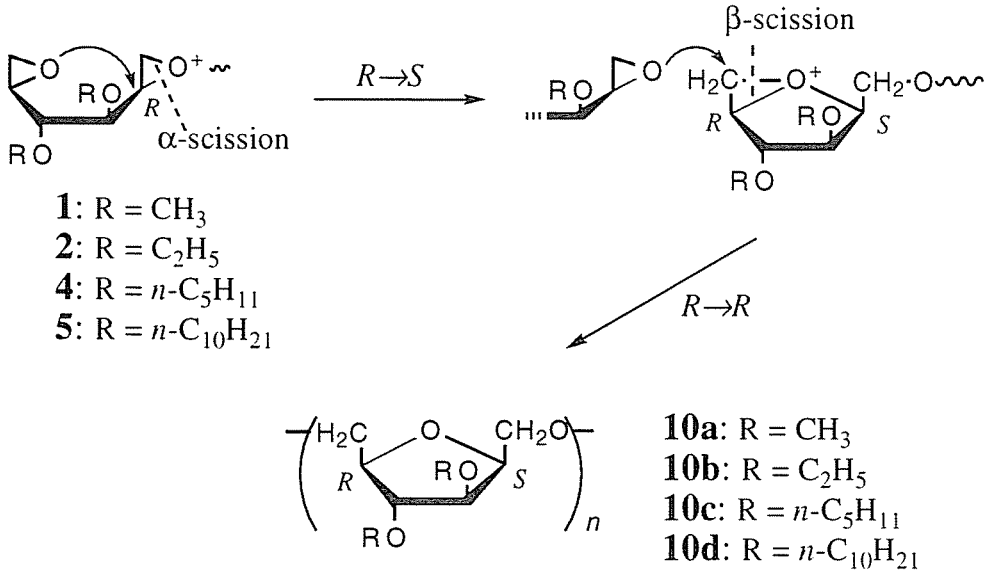
19: R=CH_3
21: R=C_2H_5

22: R=CH_3

2.3.3 Cyclopolymerization mechanism

As described in section 2.3.1, polymers **10a-d** obtained from **1**, **2**, **4** and **5** consist of 2,5-anhydro-D-glucitol recurring units, and consequently, the polymerizations proceed through β,α-scissions of two epoxide in the monomers. The mechanism of the cationic cyclopolymerization is proposed as shown in Scheme 2.8. The intramolecular cyclization occurs via the ring opening of the first epoxide with inversion (*R*→*S*) of the configuration by an S_N2 attack of the second epoxide function on the α-carbon of the former oxonium ion (α-scission). The α-scission converted D-mannitol unit in the monomers to D-glucitol unit in the polymers. The ring opening of the second epoxide takes place at the β-carbon with retention (*R*→*R*) of the configuration on the α-carbon. At the former carbon the attack is sterically favorable during the intermolecular propagation (β-scission). Therefore, polymers **10a-d** are produced through the regio- and stereoselective mechanism in the cationic cyclopolymerization of

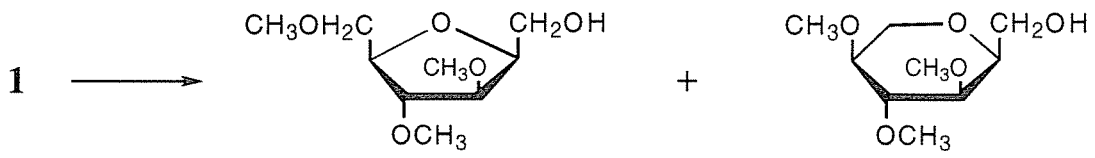
Scheme 2.8



3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitols.

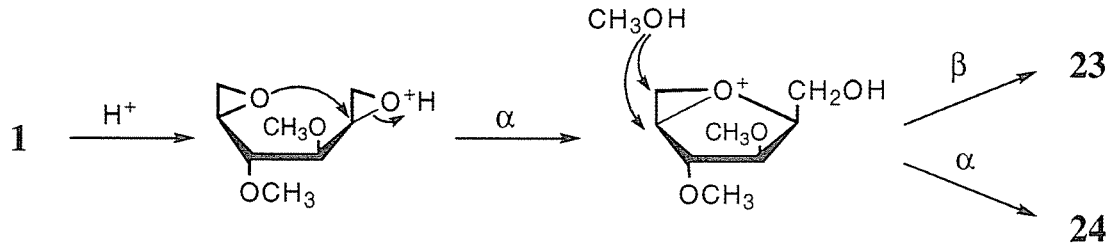
The regio- and stereoselectivity of the cyclic constitutional units in the polymer should be related to those of the cyclic unimers in the oligomer. Kuszmann reported that monomer **1** was refluxed with hydrobromic acid in water to produce 2,5-anhydro-6-bromo-6-deoxy-D-glucitol (**18**) (Scheme 2.6).[6] On the other hand, the reaction of **1** in methanol containing a catalytic amount of hydrochloric acid produced 2,5-anhydro-3,4,6-tri-*O*-methyl-D-glucitol (**23**) and 2,6-anhydro-3,4,5-tri-*O*-methyl-L-iditol (**24**) in 70 and 28 % yield, respectively (Scheme 2.9). The unimolecular cyclization is a model for the cationic cyclopolymerization.

Scheme 2.9



The cyclization can be explained by Baldwin's rule which is the general one for ring closure on the basis of the stereoelectronic effect.[7] A ring-forming process relating to epoxides is situated in the rule between tetrahedral (*Tet*) and trigonal (*Trig*) systems, generally preferring Exo-modes. The cyclizations of the 1,2:5,6-dianhydro-D-mannitols are classified into 5-Exo-*Tet* or 5-Exo-*Trig* types as a favored process and both types form 5-membered rings. For the intramolecular cyclization of **1**, the ring-opening of the protonated first epoxide, therefore, occurred at the α-carbon by attacking the second epoxide to form the 5-membered oxonium cation. Finally, methanol dominantly added to the less hindered β-carbon of the second epoxide to produce the 5-membered cyclic compound **23** as a main product, and slightly added to the more hindered α-one to produce the 6-membered one **24** as a minor product, as shown in Scheme 2.10.

Scheme 2.10



The occurrence of the regio- and stereoselectivity during the cyclization of **1** is based on Baldwin's rule, thus producing the polymer consisting of (1→6) bonded 2,5-anhydro-D-glucitol recurring units for the cyclopolymerization of 1,2:5,6-dianhydro-D-mannitols. However, small signals, which were observed in the ^{13}C NMR spectra of the polymers (Figures 2.3~2.5), indicates that polymers **10a-d** should slightly contain the 6-membered cyclic repeating units, such as 2,6-anhydro-D-glucitols corresponding to **11** in the possible cyclic units, in addition to 2,5-anhydro-D-mannitol being the main structural unit.

2.4 Conclusions

The cationic cyclopolymerization of 3,4-di-*O*-substituted 1,2:5,6-dianhydro-D-mannitol proceeded regio- and stereoselectively, and produced the polymer consisting of 2,5-anhydro-D-glucitol as a main cyclic constitutional unit and 2,6-anhydro-D-glucitol as a minor unit. After separating the polymer from the raw product, a large amount of 1,6:2,5-dianhydro-D-glucitols and a very small amount of other cyclic oligomers were isolated. On the other hand, 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol polymerized with $BF_3 \cdot OEt_2$ and $SnCl_4$ to yield the polymers with cyclic and acyclic units according to the restricted free rotation of the C-C bond at the 3,4-positions. In this case the extent of cyclization was about 0.5. The polymerizabilities of the monomers depended on the character of substituents in 3,4-positions and increased in the order of **2**>**4**>**1**>**5**≥**3**.

2.5 Experimental Section

Measurement. ^{1}H and ^{13}C NMR spectra were recorded using a JEOL JNM-A400II instrument. Optical rotation was made with a Jasco DIP-140 digital polarimeter. IR spectra were taken with a Perkin-Elmer Paragon 1000 FT-IR spectrophotometer. The molecular weights of the resulting polymers were measured by gel permeation chromatography (GPC) in tetrahydrofuran on a WATERS M45 high-performance liquid chromatograph equipped with three polystyrene gel columns (Shodex KF-804L). The number-average molecular weight (M_n) and the molecular weight distribution (M_w/M_n) were calculated on the basis of a polystyrene calibration. FI and FD-MS was obtained with a JEOL JMS-SX102A mass spectrometer.

Materials. Boron trifluoride etherate ($BF_3 \cdot OEt_2$) and tin(IV) chloride ($SnCl_4$) were purified by distillation of commercial products under reduced pressure and used as a solution in dry dichloromethane. Dichloromethane, 1,2-dichloroethane, and nitroethane were purified by the usual methods and distilled over calcium hydride. Toluene was purified by the usual methods and distilled from sodium-benzophenone. Column chromatography was performed on silica gel 60 (particle size 0.063-0.200 mm, Merck). Thin layer chromatography was performed on silica gel 60 F_{254} (0.25 mm thick, Merck).

1,2:5,6-Dianhydro-3,4-di-*O*-methyl-D-mannitol (1). Monomer **1** was prepared from D-mannitol according to the method of Kuszmann.[2] Mp 11~12 °C (Lit., mp 17~19 °C); bp 68~70 °C/0.3 mmHg (Lit., bp 95~97 °C/1.5 mmHg); $[\alpha]_D$ -9.4° and $[\alpha]_{546}$ -12.3° (*c* 1.0 in $CHCl_3$ at 22 °C) (Lit., $[\alpha]_D$ -10°, in $CHCl_3$ at 20 °C); ^{1}H NMR ($CDCl_3$): δ 3.49 (s, OCH_3, 6H), 3.13~3.16 (m, epoxy CH and CH-O, 4H), 2.86~2.93 (m, cis-CH_2, 2H), and 2.77~2.82 ppm (m, trans-CH_2, 2H); ^{13}C NMR ($CDCl_3$): δ 81.04 ($\underline{C}H$-OCH_3), 59.29 (OCH_3), 50.02 (CH) and 46.51 ppm (CH_2).

1,2:5,6-Dianhydro-3,4-di-*O*-ethyl-D-mannitol (2). Monomer **2**

was prepared from D-mannitol by the known method.[2] Bp 75-76 °C/0.25 mmHg (Lit., 67-70 °C/0.1 mmHg); $[\alpha]_D$ -6.0°, $[\alpha]_{577}$ -6.7°, $[\alpha]_{546}$ -8.7°, $[\alpha]_{435}$ -13.5°, and $[\alpha]_{405}$ -15.8° (*c* 1.0 in $CHCl_3$ at 22 °C) (Lit., $[\alpha]_D$ -6.2°, *c* 1.0 in $CHCl_3$ at 20 °C); IR (film) 2975, 2930, 2875 (CH), 1092 (COC), 846, 819 cm^{-1} (epoxy); ^1H NMR ($CDCl_3$): δ 3.84~3.46 (m, -OCH- and -OC<u>H</u>$_2$CH$_3$, 6H), 3.31~3.11 and 2.91~2.76 (m, epoxy 6H), and 1.20 ppm (t, $CH_2C\underline{H}_3$, 6H); ^{13}C NMR ($CDCl_3$): δ 79.48 (CH), 67.22 ($\underline{C}H_2CH_3$), 50.45 (epoxy CH), 46.36 (epoxy CH_2), and 15.50 ppm (CH_3).

1,2:5,6-Dianhydro-3,4-*O*-isopropylidene-D-mannitol (3). Monomer **3** was prepared from D-mannitol by the known method.[3] Bp 70-71 °C/0.6 mmHg (Lit., 69-71 °C/0.5 mmHg); $[\alpha]_D$ -2.3°, $[\alpha]_{577}$ -2.5°, $[\alpha]_{546}$ -2.9°, $[\alpha]_{435}$ -5.1°, and $[\alpha]_{405}$ -5.9° (*c* 1.0 in $CHCl_3$ at 22 °C) (Lit., $[\alpha]_D$ -2.3°, *c* 2.8 in $CHCl_3$ at 20 °C); IR (film) 2990 (ν, CH), 1059 (COC), 860 cm^{-1} (epoxy); ^1H NMR ($CDCl_3$): δ 3.84 (dd, *J*=3.2 Hz, *J*=1.5 Hz, -OCH-, 2H), 3.12~3.14 (m, epoxy CH, 2H), 2.85 (dd, *J*=4.2 Hz, *J*=4.8 Hz, epoxy CH_2, 2H), 2.73 (dd, *J*=2.6 Hz, *J*=4.8 Hz, 2H), and 1.45 ppm (s, CCH_3, 6H); ^{13}C NMR ($CDCl_3$): δ 110.27 (C), 78.18 (CH), 51.35 (epoxy CH), 45.06 (epoxy CH_2), and 26.58 ppm (CH_3).

1,2:5,6-Dianhydro-3,4-di-*O*-pentyl-D-mannitol (4). Monomer **4** was prepared by the procedure of Kuszmann.[2] Bp 105 °C/0.1 mmHg. $[\alpha]_D$ +9.3° (*c* 1.0 in $CHCl_3$ at 22 °C); ^1H NMR ($CDCl_3$): δ 0.89 (t, $^3J_{vic}$ = 7.1 Hz, 6H, pentyl-CH_3), 1.28~1.36 (br, 8H, pentyl-CH_2), 1.55~1.61 (m, 4H, -$OCH_2C\underline{H}_2$-C_3H_7), 2.79 (dd, J_{gem} = 5.3 Hz, $^3J_{trans}$ = 2.6 Hz, C1-, C6-*trans*-CH_2), 2.85 (dd, J_{gem} = 5.4 Hz, $^3J_{cis}$ = 3.8 Hz, C1-, C6-*cis*-CH_2), 3.12~3.16 (m, 2H, C2-, C5-CH), 3.26~3.30 (m, 2H, C3-, C4-CH), and 3.47~3.66 ppm (m, 4H, -OC<u>H</u>$_2$-C_4H_9, CH); ^{13}C NMR ($CDCl_3$): δ 14.00 (CH_3), 22.45, 28.10, 29.59 (CH_2), 46.13 (C1, C6), 50.54 (C2, C5), 72.01 (OCH_2), and 79.56 ppm (C3, C4).

1,2:5,6-Di-*O*-isopropylidene-D-mannitol (6). Compound **6** was prepared from D-mannitol according to the known method.[8]

3,4-Di-*O*-decyl-1,2:5,6-di-*O*-isopropylidene-D-mannitol (7). To a mixture of 36 g (0.9 mol) of sodium hydride (60 % mineral oil suspension)

in 300 mL of dry THF was added a solution of 104.8 g (0.4 mol) of 1,2:5,6-di-*O*-isopropyridene-D-mannitol in 300 mL of dry THF. After stirring for 12 h, a solution of 176.9 g (0.8 mol) of 1-bromodecane in 160 mL of dry DMSO was added, and then the mixture was stirred at 50 °C for 4 h. The reaction mixture was chilled, diluted with water, and extracted with chloroform. The extract was washed with water, dried with Na_2SO_4, and evaporated under reduced pressure. The residue was distilled to give 94 g (43.4 % yield) of **7**. Bp 170 °C/6x10^{-5} mmHg; $[\alpha]_D$ +14.4° (*c* 1.0 in $CHCl_3$ at 22 °C); R_f 0.29 (ethyl acetate/*n*-hexane, 1/10); ^{1}H NMR ($CDCl_3$): δ 0.88 (t, $^3J_{vic}$ = 6.8 Hz, 6H, CH_3), 1.27 (s, 28H, CH_2), 1.38 (s, 12H, $C(CH_3)_2$), 1.54~1.57 (m, 4H, -$OCH_2\underline{CH_2}$-C_8H_{17}), 3.52 (d, $^3J_{vic}$ = 6.1 Hz, 2H, C3-, C4-CH), 3.56~3.62 (m, 4H, -$OC\underline{H_2}$-C_9H_{19}), 3.92 (dd, J_{gem} = 8.2 Hz, $^3J_{cis}$ = 6.6 Hz, C1-, C6-cis-CH_2), 4.08 (dd, J_{gem} = 8.2 Hz, $^3J_{trans}$ = 6.2 Hz, C1-, C6-trans-CH_2), and 4.19 ppm (q, *J* = 6.25 Hz, 2H, C2-, C5-CH); ^{13}C NMR ($CDCl_3$): δ 14.11 (CH_3), 22.68, 26.08 ($C(\underline{C}H_3)_2$), 25.43, 26.72, 29.32, 29.52, 29.59, 31.89 (CH_2), 30.31 ($OCH_2\underline{C}H_2$-C_8H_{17}), 66.81 (C1, C6), 73.42 (-$O\underline{C}H_2$-C_9H_{19}), 75.81 (C2, C5), 80.40 (C3, C4), and 108.45 ppm ($\underline{C}(CH_3)_2$); Anal. Calcd for $C_{32}H_{62}O_6$ (542.84): C, 70.80; H, 11.51. Found: C, 70.79; H, 11.69.

3,4-Di-*O*-decyl-D-mannitol (8). A solution of 23.2 g (43 mmol) of **7** in 116 mL of acetic acid and 58 mL of water was refluxed for 30 min. After cooling, the mixture was evaporated under reduced pressure. The residue was diluted with water and evaporated under reduced pressure. This procedure was repeated until the odor of acetic acid disappeared. The residue was recrystalized from ethyl acetate to give 13.7 g (69.5 % yield) of **8** having mp 93 °C. R_f 0.57 (methanol/chloroform, 1/5); $[\alpha]_D$ +26.7° (*c* 1.0 in CH_3OH at 22 °C); ^{1}H NMR ($CDCl_3$): δ 0.90 (t, $^3J_{vic}$ = 6.9 Hz, 6H, CH_3), 1.25~1.40 (br, 28H, CH_2), 1.53~1.59 (m, 4H, -$OCH_2\underline{CH_2}$-C_8H_{17}), 3.30~3.37 (m, 4H, -$OC\underline{H_2}$-C_9H_{19}), 3.56~3.75 (m, 10H, C1-, C6-CH_2, C2-, C3-, C4-, C5-CH), and 3.80 ppm (dd, 2H, *J* = 11.1 Hz, *J* = 2.7 Hz, C1-, C6-CH_2); ^{13}C NMR ($CDCl_3$): δ 14.77 (CH_3), 24.03, 27.59, 30.77, 31.01, 32.67 (CH_2), 31.70 (-$OCH_2\underline{C}H_2$-C_8H_{17}), 65.00 (C1, C6), 74.20 (-$O\underline{C}H_2$-

C_9H_{19}), 72.70 (C2, C5), and 80.36 ppm (C3, C4). Anal. Calcd for $C_{26}H_{54}O_6$ (462.71): C, 67.49; H, 11.76. Found: C, 66.90; H, 11.93.

3,4-Di-*O*-decyl-1,6-di-*O*-*p*-toluenesulfonyl-D-mannitol (9). To a solution of 12.7 g (27 mmol) of **8** in 50 mL of pyridine was added 11.3 g (59 mmol) of *p*-toluenesulfonyl chloride at 0 °C. After stirring at 0 °C for 0.5 h and then at room temperature for 0.5 h, water was added, and the mixture was extracted with chloroform. The extracts were washed with diluted hydrochloric acid, dried under Na_2SO_4, and evaporated under reduced pressure. The residue was chromatographed on silica gel with ethyl acetate/*n*-hexane (1/7) to give 17.8 g (80.2 % yield) of **9**. R_f: 0.30; $[\alpha]_D$ +16.3 (*c* 1.0 in $CHCl_3$ at 22 °C); ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 6H, CH_3), 1.26 (s, 28H, CH_2), 1.43~1.48 (m, 4H, $OCH_2C\underline{H}_2$-C_8H_{17}), 2.45 (s, 6H, $PhCH_3$), 3.40~3.62 (m, 6H, -$OC\underline{H}_2$-C_9H_{19}, CH), 3.96~4.01 (m, 2H, CH), 4.17~4.19 (m, 4H, C1-, C6-CH_2), 7.34~7.37 (m, 4H, Ph), and 7.79~7.82 ppm (m, 4H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.10 (CH_3), 22.66 ($Ph\underline{C}H_3$), 25.90, 29.30, 29.56, 31.88 (CH_2), 31.70 (-$OCH_2\underline{C}H_2$-C_8H_{17}), 69.46, 76.60 (CH), 71.11 (C1, C6), 72.95 (-$O\underline{C}H_2$-C_9H_{19}), 128.03, and 129.90 ppm (Ph). Anal. Calcd for $C_{40}H_{66}O_{10}S_2$ (771.09): C, 62.31; H, 8.63; S, 8.32. Found: C, 61.46; H, 8.71; S, 8.00.

1,2:5,6-Dianhydro-3,4-di-*O*-decyl-D-mannitol (5). A mixture of 18.8 g (24 mmol) of **9** and 3.2 g of ground KOH in 100 mL of ether was vigorously stirred under reflux for 1 h. After the mixture cooled, the precipitates were removed by filtering the mixture through a pad of Celite, and then the filtrate was evaporated under reduced pressure. The residue was distilled under reduced pressure to give 2.2 g (22.1 % yield) of **5** as a colorless liquid. Bp 120 °C/6x10^{-5} mmHg; R_f: 0.3 (ethyl acetate/*n*-hexane, 1/7); $[\alpha]_D$ +6.8° (c = 1.0 in $CHCl_3$ at 22 °C); ^{1}H NMR ($CDCl_3$): δ 0.88 (t, $^3J_{vic}$ = 6.9 Hz, 6H, decyl-CH_3), 1.21~1.31 (br, 28H, decyl-CH_2), 1.54~1.62 (m, 4H, -$OCH_2C\underline{H}_2$-C_8H_{17}), 2.79 (dd, J_{gem} = 5.4 Hz, $^3J_{trans}$ = 2.7 Hz, C6-CH_2), 2.85 (dd, J_{gem} = 5.4 Hz, $^3J_{cis}$ = 3.9 Hz, C6-CH_2), 3.13~3.16 (m, 2H, C2, C5-$C\underline{H}_2$), 3.26~3.28 (m, 2H, C3-,

C4-CH), 3.46 (dd, 2H, J_{gem} = 9.3 Hz, $^{3}J_{vic}$ = 6.9 Hz, -OC$\underline{H}_2$-C_9H_{19}), and 3.67 ppm (dd, 2H, J_{gem} = 9.3 Hz, $^{3}J_{vic}$ = 6.6 Hz, -OC$\underline{H}_2$-C_9H_{19}); ^{13}C NMR ($CDCl_3$): δ 14.08 (CH_3), 22.64, 25.96, 29.29, 29.41, 29.54, 29.57, 31.88 (CH_2), 29.92 ($OCH_2\underline{C}H_2$-C_8H_{17}), 46.11 (C1, C6), 50.54 (C2, C5), 72.03 (-O$\underline{C}H_2$-C_9H_{19}), and 79.56 ppm (C3, C4). Anal. Calcd for $C_{26}H_{50}O_4$ (426.69): C, 73.18; H, 11.82. Found: C, 73.01; H, 11.83.

2,5-Anhydro-3,4-di-*O*-methyl-D-glucitol (16). The mixture of **1** (1.74 g, 10 mmol) and 40 mL of water was heated under reflux for 7 h and then the solution was evaporated under reduced pressure to obtain a syrup from which the water had been removed by two azeotropic distillations with benzene and chloroform. The syrup was purified by flash column chromatography using ethyl acetate/isopropanol (5/1). The fractions having an R_f 0.5 gave, on evaporation, pure **16** as a colorless syrup (1.57 g, 81.8 %). $[\alpha]_{546}$ +88.1°(*c* 1.0 in $CHCl_3$ at 22 °C); IR (film): 3370 (OH), 2920, 2870, 2810 (ν, C-H), and 1085 cm^{-1} (ν_{as}, C-O-C); ^{1}H NMR ($CDCl_3$): δ 4.08 (dt, *J*= 4.9 Hz, *J*= 4.4 Hz, H2, 1H), 3.91 (td, *J*= 4.4 Hz, *J*= 3.2 Hz, H5, 1H), 3.80~3.88 (m, H3, H1, H6A, 4H), 3.81 (dd, *J*= 4.3 Hz, *J*= 2.1 Hz, H4, 1H), 3.69 (dd, *J*= 11.9 Hz, *J*= 4.3 Hz, H6B, 1H), 3.43 (s, CH_3O, 6H), and 3.15 ppm (br s, HO, 2H); ^{13}C NMR ($CDCl_3$): δ 86.19 (C3), 84.37 (C4), 83.52 (C5), 80.26 (C2), 62.78 (C6), 61.42 (C1), 57.63 (CH_3O), and 57.50 ppm (CH_3O).

2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol (14). To a stirred solution of **16** (1.44 g, 7.5 mmol) in 9.6 mL of dimethyl sulfoxide was simultaneously added a solution of sodium hydroxide (1.5 g, 37.5 mmol) in 1.5 mL of water and dimethyl sulfate (2.40 g, 19 mmol) at such a rate that 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 the residue was purified by column chromatography with *n*-hexane/diethyl ether (1/1). Evaporation of the fractions having an R_f

0.45 gave pure **14** as a colorless syrup (0.78 g, 47.3 %). $[\alpha]_D$ +66.7°, $[\alpha]_{577}$ +69.8°, $[\alpha]_{546}$ +78.6°, $[\alpha]_{435}$ +130.1°, and $[\alpha]_{405}$ +155.4° (*c* 1.06 in $CHCl_3$ at 20 °C); IR (film): 2975, 2900, 2890, 2810 (ν, C-H), and 1100 cm^{-1} (ν_{as}, C-O-C); ^1H NMR ($CDCl_3$): δ 4.09 ($^3J_{H6A,\ H5}$ = 6.8 Hz, $^3J_{H6B,\ H5}$ = 5.0 Hz, $^3J_{H5,\ H4}$ = 4.3 Hz, H5, 1H), 3.92 ($^3J_{H2,\ H1A}$ = 5.9 Hz, $^3J_{H2,\ H1B}$ = 5.9 Hz, $^3J_{H2,\ H3}$ = 3.6 Hz, H2, 1H), 3.68 ($^3J_{H4,\ H5}$ = 4.1 Hz, $^3J_{H4,\ H3}$ = 0.8 Hz, H4, 1H), 3.64 ($^3J_{H3,\ H2}$ = 3.9 Hz, $^3J_{H3,\ H4}$ = 1.2 Hz, H3), 3.64 (A) and 3.59 (B) ($^3J_{H6A,\ H5}$ = 6.8 Hz, $^3J_{H6B,\ H5}$ = 5.0 Hz, $^2J_{H6A,\ H6B}$ = 10.2 Hz, H6, 2H), 3.55 (A) and 3.47 (B) ($^3J_{H1A,\ H2}$ = 6.0 Hz, $^3J_{H1B,\ H2}$ = 5.9 Hz, $^2J_{H1A,\ H1B}$ = 10.0 Hz, H1, 2H), 3.40 (CH_3O on C1), 3.40 (CH_3O on C6) 3.39 (CH_3O on C4), and 3.38 ppm (CH_3O on C3); ^{13}C NMR ($CDCl_3$): δ 85.69 (C3), 84.75 (C4), 82.26 (C2), 79.83 (C5), 73.15 (C1), 70.66 (C6), 59.25 and 59.19 (CH_3O on C6 and C1), 57.42 and 57.35 ppm (CH_3O on C3 and C4); Anal. Calcd for $C_{10}H_{20}O_5$: C, 54.53; H, 9.15. Found: C, 53.97; H, 9.25.

2,5-Anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol (15). Compound **15** was prepared from **2** according to the known method.[1] Compound **2** was refluxed in water to yield 2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol (**17**), and then **17** was treated with dimethyl sulfate to give **15**, as described for **14**.

1,6:2,5-Dianhydro-3,4-di-*O*-methyl-D-glucitol (19). Compound **19** was prepared from **1** according to the known method. R_f = 0.35 (*n*-hexane/ethyl acetate = 1/1); $[\alpha]_D$ -19.2°, $[\alpha]_{577}$ -20.2°, $[\alpha]_{546}$ -22.8°, $[\alpha]_{435}$ -39.3°, and $[\alpha]_{435}$ -47.6° (*c* 1.0, $CHCl_3$ at 22 °C) (Lit., $[\alpha]_D$ -22.5°, in $CHCl_3$ at 20 °C); ^1H NMR ($CDCl_3$): δ 4.24 (br d, *J* = 6.1 Hz, H2, 1H), 4.01 (s, H5, 1H), 4.00 (s, H4, 1H), 3.93 (ddd, *J* = 6.3 Hz, *J* = 1.3 Hz, *J* = 1.0 Hz, H3, 1H), 3.84 (dd, *J* = 11.5 Hz, *J* = 1.7 Hz, H6, 1H), 3.79 (d, *J* = 1.5 Hz, H1, 2H), 3.66 (dt, *J* = 11.6 Hz, *J* = 1.0 Hz, H6, 1H), 3.49 (s, CH_3O, 3H), and 3.41 ppm (s, CH_3O, 3H); ^{13}C NNR ($CDCl_3$) δ 87.70 (C4), 87.64 (C3), 79.05 (C5), 76.37 (C2), 69.20 (C1), 65.43 (C6), 58.58 (OCH_3), and 56.88 ppm (OCH_3); IR (film): 2940, 2900, 2850, 2825, 1216, 1110, 1104, 1070, and 885cm^{-1}.

2,5-Anhydro-6-bromo-6-deoxy-3,4-di-*O*-ethyl-D-glucitol (20). Compounds **20** and **21** were prepared by the procedure similar to that described by Kuszmann.[6] A solution of **2** (2.02 g, 10 mmol) in acetone (5 mL) was added dropwise to an ice-cold, stirred solution of conc. hydrobromic acid (2 mL) in water (2 mL). The mixture was stirred for 15 min at room temperature, and was then made neutral with solid sodium hydrogen carbonate. The precipitated salts were filtered off, and the filtrate was then evaporated. The residue was added EtOH and was filtered off. The clear filtrate was evaporated, and the residual oil was purified by column chromatography with ethyl acetate/dichloromethane (1/2). Evaporation of the fractions having R_f 0.43 gave 2.40 g (84.8 % yield) of pure **20**. $[\alpha]_{577}$ +3.3°, $[\alpha]_{546}$ +4.6°, $[\alpha]_{435}$ +6.9°, and $[\alpha]_{405}$ +7.7° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{1}H NMR ($CDCl_3$): δ 4.17 (q, *J*= 4.5 Hz, H2, 1H), 4.07~4.11 (ddd, *J* = 2.6 Hz, *J* = 5.5 Hz, *J* = 8.0 Hz, H5, 1H), 3.91~3.94 (m, H3 and H4, 2H), 3.81~3.90 (m, H1, 2H), 3.56~3.71 (m, ethyl CH_2, 4H), 3.45~3.55 (m, H6, 2H), 2.47 (br, OH, 1H), and 1.22 (dt, *J* = 2.4 Hz, *J* = 7.0 Hz, ethyl CH_3, 6H); ^{13}C NMR ($CDCl_3$): δ 84.50, 84.40, 82.47, 81.08, 65.78 (ethyl CH_2), 65.26 (ethyl CH_2), 61.78 (C1), 32.55 (C6), and 15.36 ppm (ethyl CH_3); Anal. Calcd for $C_{10}H_{19}O_4Br$: C, 42.40; H, 6.77; Br, 28.23. Found: C, 42.66; H, 6.75; Br, 28.43.

1,6:2,5-Dianhydro-3,4-di-*O*-ethyl-D-glucitol (21). A mixture of **20** (2.40 g, 8.5 mmol) and 0.5M potassium 1-butoxide in 1-butanol (19.5 mL) was heated at 100 °C for 1 h. The cooled solution was made neutral with diluted hydrochloric acid, and then evaporated. The residue was dissolved in chloroform, and the solution washed with water, dried, and evaporated. The residue was purified by column chromatography with ethyl acetate/*n*-hexane (2/3). Evaporation of the fractions having R_f 0.43 gave 0.96 g (56.0 % yield) of pure **21**. $[\alpha]_D$ -28.8°, $[\alpha]_{577}$ -33.3°, $[\alpha]_{546}$ -37.7°, $[\alpha]_{435}$ -64.9°, and $[\alpha]_{405}$ -78.2° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{1}H NMR ($CDCl_3$): δ 4.21 (br d, *J*= 6.3 Hz, H2, 1H), 4.10 (d, *J*= 2.4Hz, H4,1H), 4.03 (ddd, *J*= 0.9 Hz, *J*= 2.4 Hz, *J*= 6.3 Hz, H3, 1H), 3.98

(br s, H5, 1H), 3.83 (dd, J= 1.6 Hz, J= 11.4 Hz, H6, 1H), 3.79 (d, J= 1.4 Hz, H1, 2H), 3.49~3.73 (m, H6 and ethyl CH_2, 5H), and 1.26 ppm (dt, J= 2.9 Hz, J= 6.9 Hz, ethyl CH_3, 6H); ^{13}C NMR ($CDCl_3$): δ 86.35 (C3), 86.25 (C4), 79.52 (C5), 76.56 (C2), 69.24 (C6), 66.46 (ethyl CH_2), 65,57 (C1), 64.82 (ethyl CH_2), 15.41 (ethyl CH_3), and 15.27 ppm (ethyl CH_3); Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97. Found: C, 59.62; H, 9.61; FI-MS: m/z (relative intensity): 202 (M^+-100), 203 (MH^+-13.5), and 204 (2.5).

Oligomer separation. After separating the *n*-hexane-insoluble polymer from the polymerization products of **1**, the filtrate was evaporated, and the residue was purified by thin layer chromatography with ethyl acetate/*n*-hexane (1/1). Evaporation of the fractions having an R_f 0.48 gave 150 mg (30.0 % yield) of the compound whose ^1H and ^{13}C NMR spectra and physical properties were identical with those of **19**. FI-MS: m/z (relative intensity): 174 (M^+ 100), 175 ($(M+1)^+$ 10.7), and 176 (2.0).

Evaporation of the fractions having an R_f 0.25 gave 30 mg (yield, 6 %) of compound **22**. $[\alpha]_{577}$ -2.4°, $[\alpha]_{546}$ -4.2°, $[\alpha]_{435}$ -6.4°, and $[\alpha]_{435}$ -7.2° (*c* 1.0, $CHCl_3$ at 23 °C); ^1H NMR ($CDCl_3$): δ 4.53 (dd, J = 8.2 Hz, J = 7.9 Hz, H4, 1H), 4.20 (dd, J = 7.9 Hz, J = 2.6 Hz, H2, 1H), 4.03 (dd, J = 8.2 Hz, J = 7.9 Hz, H3, 1H), 3.79 (s, H6, 1H), 3.76 (dd, J = 6.3 Hz, J = 2.3 Hz, H5, 1H), 3.54~3.67 (m, H1 and H6, 2H), 3.52 (s, CH_3O-, 3H), 3.47 (s, CH_3O-, 3H), and 3.35~3.46 ppm (m, H1, 1H); ^{13}C NMR ($CDCl_3$) δ 85.59 (C3), 82.19 (C4), 79.91 (C5), 76.50 (C2), 70.82 (C6), 69.74 (C1), 58.78 (OCH_3), and 56.62 ppm (OCH_3); FI-MS: m/z (relative intensity): 348 (M^+ 100), 349 ($(M+1)^+$ 55.2), and 350 (17.5).

The isolation of the *n*-hexane-soluble products in the polymerization of **2**: After the polymerization products were poured into *n*-hexane, the *n*-hexane solusion was evaporated, and the residue was purified by thin layer chromatography with ethyl acetate/*n*-hexane (2/3). Evaporation of the fractions having R_f 0.43 gave 327 mg (65.3 % yield) of the compound whose ^1H and ^{13}C NMR spectra and physical properties were identical with those of **21**.

Model cyclization. A solution of **1** (0.5 g, 2.87 mmol) in methanol containing a drop of hydrochloric acid was stirred at room temperature for 24 h. The mixture was neutralized by adding methanolic sodium methoxide and then evaporated under reduced pressure. The residue was purified by column chromatography to yield 2,5-anhydro-3,4,6-tri-*O*-methyl-D-glucitol (**23**) (0.41 g, 70 %) and 2,6-anhydro-3,4,5-tri-*O*-methyl-L-iditol (**24**) (0.16 g, 28 %). **23**; $[\alpha]_D$ +54.7°, $[\alpha]_{577}$ +57.0°, $[\alpha]_{546}$ +64.1°, $[\alpha]_{435}$ +105.3°, and $[\alpha]_{405}$ +123.3° (*c* 1.0 in $CHCl_3$ at 23°C); ^{1}H NMR ($CDCl_3$): δ = 4.08 (dt, *J*= 4.9 Hz, *J*= 4.8 Hz, H2, 1H), 3.92 (td, *J*= 5.0 Hz, *J*= 4.9 Hz, H5, 1H), 3.84 (dd, *J*= 5.1 Hz, *J*= 2.7 Hz, H3, 1H), 3.82 (br d, *J* = 4.2 Hz, H1, 2H), 3.74 (dd, *J* = 4.7 Hz, *J* = 2.8 Hz, H4, 1H), 3.55 (d, *J*= 5.4 Hz, H6, 2H), 3.43 (s, -OCH_3 on C3 and C4, 6H), 3.42 (s, -OCH_3 on C6, 3H), and 2.70 ppm (br s, OH, 1H); ^{13}C NMR ($CDCl_3$): δ 86.04 (C3), 84.97 (C4), 81.32 (C5), 80.06 (C2), 73.20 (C6), 61.47 (C1), 59.25 (-OCH_3 on C6), 57.71 and 57.65 ppm (-OCH_3 on C3 and C4); Anal. Calcd for $C_9H_{18}O_5$: C, 52.41; H, 8.80. Found: C, 51.63; H, 8.75; FI-MS: *m/z* (relative intensity): 206 (M^+-40.6), 207 (MH^+-100), 208 (15.9), 413 ($(2M+H)^+$-40.2), and 414 (12.1). **24**; $[\alpha]_D$ +39.3°, $[\alpha]_{577}$ +42.5°, $[\alpha]_{546}$ +48.0°, $[\alpha]_{435}$ +80.4°, and $[\alpha]_{405}$ +93.4° (*c* 1.0 in $CHCl_3$ at 23°C); ^{1}H NMR ($CDCl_3$): δ 3.89~3.96 (m, H1 and H6, 2H), 3.75~3.80 (m, H5, 1H), 3.72 (dd, *J* = 12.4 Hz, *J* = 2.7 Hz, H1, 1H), 3.67 (dd, *J* = 11.5 Hz, *J* = 4.1 Hz, H6, 1H), 3.56 (t, *J* = 3.9 Hz, H3, 1H), 3.48 (s, -OCH_3, 3H), 3.45 (s, -OCH_3, 3H), 3.44 (s, -OCH_3, 3H), 3.25-3.28 (m, H4, 1H), 3.19~3.23 (m, H2, 1H), and 2.41 ppm (br s, OH, 1H); ^{13}C NMR ($CDCl_3$): δ 76.85 (C4), 76.09 (C2), 75.53 (C5), 74.59 (C3), 64.43 (C6), 61.78 (C1), 58.39 (-OCH_3), 57.71 (-OCH_3) and 57.62 ppm (-OCH_3); Anal. Calcd for $C_9H_{18}O_5$: C, 52.41; H, 8.80. Found: C, 51.97; H, 8.78; FI-MS: *m/z* (relative intensity): 206 (M^+-100), 207 (MH^+-37.8), 208 (5.6), and 413 ($(2M+H)^+$-7.1).

Typical polymerization procedure. All the polymerizations were carried out in side-armed ampoules, and BF_3•OEt_2 and $SnCl_4$ were used as a solution in dichloromethane. At the end of the polymerization, the reaction

mixture was poured into a large amount of methanol. The resulting polymers from **1~3** were purified by reprecipitation from chloroform-*n*-hexane and the polymers from **4** and **5** were purified by reprecipitation from methanol-*n*-hexane.

A typical polymerization procedure is as follows. Monomer **1** (500 mg, 2.87 mmol) was dissolved in dry CH_2Cl_2 (5.74 mL), and then $BF_3 \cdot OEt_2$ (3.62 μL, 0.0287 mmol) was added using a microsyringe. After 24 h at 0 °C, the solution was poured into a large amount of methanol containing a drop of aqueous ammonia, and the solvent was then evaporated under reduced pressure. The residue was washed using *n*-hexane and dried under vacuum to give 245 mg (48.9 % yield) of the polymer; the M_n and M_w/M_n were 2650 and 2.03, respectively. $[\alpha]_D$ +32.8 °, $[\alpha]_{577}$ +36.2°, $[\alpha]_{546}$ +41.3°, $[\alpha]_{435}$ +69.3°, and $[\alpha]_{405}$ +82.5° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR ($CDCl_3$): δ 85.41 (CH), 84.68 (CH), 82.27 (CH), 79.86 (CH), 71.72 (CH_2), 69.32 (CH_2), and 57.32 ppm (OCH_3).

The polymerization of **2** in CH_2Cl_2 using $BF_3 \cdot OEt_2$ gave 104 mg (20.7 % yield) of the polymer. The M_n and M_w/M_n were 6140 and 1.66, respectively. $[\alpha]_D$ +35.2 °, $[\alpha]_{577}$ +37.6°, $[\alpha]_{546}$ +42.7°, $[\alpha]_{435}$ +71.9°, and $[\alpha]_{405}$ +85.7° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR ($CDCl_3$): δ 84.32 (CH), 83.13 (CH), 82.44 (CH), 79.84 (CH), 71.85 (CH_2), 69.39 (CH_2), 65.04 (ethyl CH_2) and 15.35 ppm (ethyl CH_3).

The polymerization of **3** in CH_2Cl_2 using $BF_3 \cdot OEt_2$ gave 198 mg (39.5 % yield) of the polymer. The M_n and M_w/M_n were 2000 and 1.63, respectively. $[\alpha]_D$ +6.4 °, $[\alpha]_{577}$ +6.6°, $[\alpha]_{546}$ +7.6°, $[\alpha]_{435}$ +10.6°, and $[\alpha]_{405}$ +13.9° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR ($CDCl_3$): δ 109.70, 79.32, 79.15, 74.49, 63.49, 52.11, 43.83, 27.16, and 26.74 ppm.

Monomer **4** (500 mg, 1.75 mmol) was dissolved in dry CH_2Cl_2 (3.50 mL), and a solution of $BF_3 \cdot OEt_2$ in CH_2Cl_2 (24.8 μL in 0.70 mol•L^{-1}, 0.0175 mmol) was added using a microsyringe at 0 °C. After 24 h, the reaction mixture was poured into a large amount of methanol containing a drop of aqueous

ammonia, and the entire solution was evaporated under reduced pressure. The residue was extracted using *n*-hexane/MeOH and the MeOH layer was evaporated under reduced pressure. This procedure was repeated several times until the monomer in MeOH phase disappeared in the GPC trace. (158 mg, 31.6 %). The M_n and M_w/M_n were 6200 and 1.98, respectively. $[\alpha]_D$ +19.7° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR ($CDCl_3$) δ 14.02 (CH_3), 22.46, 22.50 (-$\underline{C}H_2CH_3$), 28.33, 28.37 (-OC_2H_4-$\underline{C}H_2$-C_2H_5), 29.48, 29.54 (-$OCH_2\underline{C}H_2$-C_3H_7), 69.39 (C6) 69.77, 69.89 (-OCH_2), 71.96 (C1), 79.97 (C5), 82.44 (C2), 83.26 (C4), and 84.38 ppm (C3).

The polymerization of **5** in CH_2Cl_2 using BF_3•OEt_2 gave 231 mg (46.2 % yield) of the polymer. The M_n and M_w/M_n were 3920 and 1.41, respectively. $[\alpha]_D$ +13.3 °, $[\alpha]_{577}$ +14.1°, $[\alpha]_{546}$ +16.0°, $[\alpha]_{435}$ +26.7°, and $[\alpha]_{405}$ +31.6° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR ($CDCl_3$) δ 14.09 (CH_3), 22.68, 26.19, 29.35, 29.62, 29.83 (CH_2), 31.91 (-$OCH_2\underline{C}H_2$-C_8H_{17}), 69.32 (C6), 69.81, 69.96 (-$O\underline{C}H_2$-C_9H_{19}), 72.00 (C1), 79.91 (C5), 82.38 (C2), 83.24 (C4) and 84.45 (C3).

2.6 References

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Highly Regio- and Stereoselective Cyclopolymerization of 1,2:5,6-Dianhydro-3,4-di-*O*-alkyl-D-mannitols using Anionic Catalysts

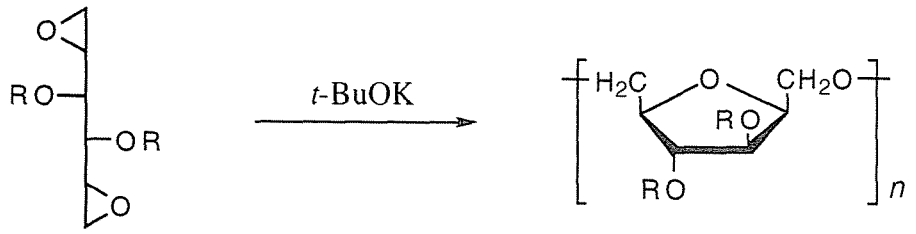
3.1 Introduction

In previous chapter, 3,4-di-*O*-alkyl substituted 1,2:5,6-dianhydro-D-mannitols (**1**, **2**, **4** and **5**) were found to polymerize using cationic initiators. The resulting polymers consisted of 2,5-anhydro-D-glucitols as the main repeating units together with other cyclic units being minor components. The cationic cyclopolymerization is regio- and stereoselective, and noteworthy as a new method of synthesizing polysaccharides. The polymerization method, however, requires extensive improvements in the relatively low polymer yield, the formation of oligomers, and the difficulty in giving the polymers with certain molecular weights. The structural characteristic of (1→6) linked 2,5-anhydro-D-glucitol is a lack of the anomeric linkage which is found in the naturally occurring polysaccharides. Chapter **3** focuses on the cyclopolymerization of 1,2:5,6-dianhydro-D-mannitols using an anionic initiator in order to prepare the polysaccharide consisting of the distinct (1→6) linked 2,5-anhydro-D-glucitol and having the satisfactory molecular weight.

The chapter describes the cyclopolymerization of **1**, **4** and **5** using potassium *tert*-butoxide and potassium hydroxide as the anionic initiator. In addition, to activate the catalyst and the growing chain end, the anionic polymerization of **1** is performed in the presence of 18-crown-6. The polymerization of **3** is also carried out in order to clarify the substituent effect at the 3,4-position. The regio- and stereoselectivities of the

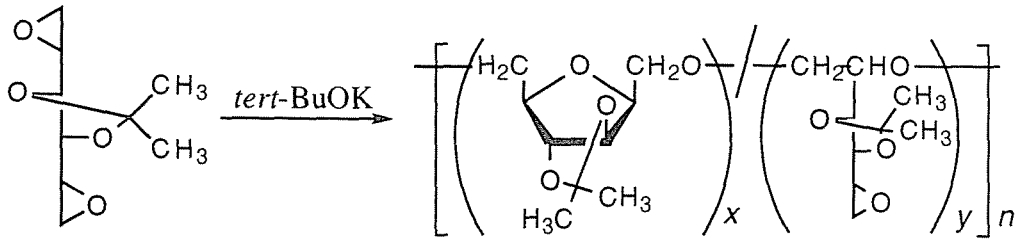
cyclopolymerizations of **1**, **3**, **4** and **5** are discussed by comparing the spectral characteristics of the resulting polymers with those of the cyclic model compounds (**14**, **23**, **26** and **27**). 1,2:5,6-Dianhydro-3,4-*O*-isopropylidene-D-mannitol (**3**), which was polymerized with cationic initiators to yield polymers with cyclic and acyclic units, is also studied on the anionic polymerization (Scheme 3.1).

Scheme 3.1



1: R = CH_3
4: R = *n*-C_5H_{11}
5: R = *n*-$C_{10}H_{21}$

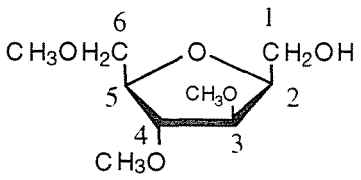
25a: R = CH_3
25b: R = *n*-C_5H_{11}
25c: R = *n*-$C_{10}H_{21}$



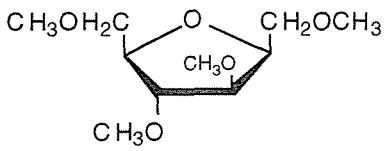
3

25d

Chart 3.1



23



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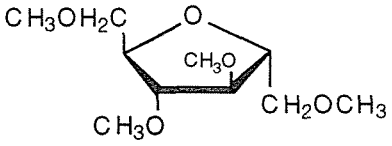
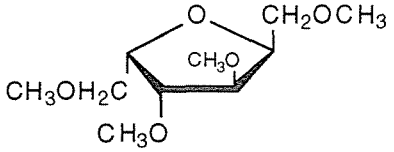


26



27

3.2 Results

3.2.1 Anionic polymerization of 1,2:5,6-dianhydro-3,4-di-O-methyl-D-mannitol

Table 3.1 summarizes the results of the polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) using *t*-BuOK and KOH at 60°C. All the polymerizations proceeded homogeneously, until the monomers were completely consumed. The reaction system always exhibited a color change from colorless to dark brown as the reaction progressed. The obtained polymers were a yellow-brown sticky semisolid, and soluble in toluene, chloroform, tetrahydrofuran, methanol, and water but insoluble in *n*-hexane. The polymers were similar in solubility to those obtained with cationic initiators.

For the polymerization with a [**1**]/[*t*-BuOK] molar ratio of 20, the yields and the number-average molecular weights (M_ns) of polymers gradually increased with prolonging polymerization time. After the polymerization for 48 h, the conversion came close to 100%. This polymerization in which the M_n increases with conversion shows typical characteristics of the stepwise anionic polymerization of alkylene oxides. The ultimate M_n of the polymer varied with

Table 3.1. Anionic polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (1)[a]

Catalyst	[1]/[Cat.]	Solvent	Time h	Yield %	M_n [b]	M_w/M_n [b]	DP_n	$[\alpha]_{546}^{23}$ [c]
t-BuOK	2	Toluene	48	52.1[d]	1100	1.09	6.3	+69.4
	5	Toluene	48	96.5	1590	1.27	9.1	+76.2
	10	Toluene	48	97.0	3030	1.41	17.4	+79.8
	20	Toluene	1	23.0	2110	1.22	12.1	+72.8
	20	Toluene	2	37.4	3070	1.28	17.6	+65.3
	20	Toluene	6	62.9	4140	1.30	23.8	+68.8
	20	Toluene	12	75.7	4930	1.43	28.3	+66.1
	20	Toluene	48	98.5	6410	1.53	36.8	+84.5
	40	Toluene	48	94.1	12900	1.65	74.1	+72.2
	20	Benzene	48	95.4	6400	1.64	36.8	+84.9
	20	1,4-Dioxane	48	96.1	7960	1.48	45.7	+93.9
	20	THF	48	84.3	5100	1.31	29.3	+78.0
	20[e]	Toluene	48	92.5	2980	1.38	17.1	+90.4
KOH	5	THF	100	69.5	7680	1.91	44.1	+70.5
	5	Toluene	60	44.8	3860	1.76	22.1	+74.0
	10	Toluene	60	21.4	4260	1.75	24.5	+75.5

[a] [**1**]=1.0 mol•L^{-1}; temp, 60℃. [b] Measured in THF by GPC using polystyrene as the standard. [c] *c* 1.0 in chloroform. [d] Perhaps some low molecular weight polymer was lost in the precipitation. [e] [crown]/[*t*-BuOK]=2.0; 18-crown-6 in the polymer was removed by reprecipitation from chloroform-*n*-butyl ether.

the molar ratio of monomer to initiator, and a linear relationship between them was found. When the [**1**]/[*t*-BuOK] molar ratio of 40 was used for 48h in toluene, the M_n of the polymer attained 12900 (DP_n = 74), which was almost twice that of the polymer from the [**1**]/[*t*-BuOK] molar ratio of 20. The degree of polymerization was larger than that estimated from the molar ratio, thus resulting in an initiator efficiency of about 55%. The reason for the loss of initiator is obscure. The M_n was slightly increased with decreasing dipole moment of the solvent by which the chain transfer reaction should be depressed. The molecular weight distribution (M_w/M_n) was relatively narrow with a value

in the rang of 1.09~1.65. For the anionic polymerization, the M_n of the obtained polymer was higher than those for the cationic polymerization using $BF_3 \cdot OEt_2$. The specific rotation of the polymer varied in the range of +65.3° to +93.9°. However, the obvious relation between the specific rotation and the M_n was not observed.

KOH was also effective for converting monomer **1** to a gel-free polymer, but was not as active as *t*-BuOK. The rate of polymerization was rather slow, and the polymerization was not complete even after a long time of 100 h. The M_n was far larger than that estimated from the [**1**]/[KOH] molar ratio. These results are interpreted as being caused by the lower basicity and solubility of KOH in comparison with *t*-BuOK.

The addition of crown ether was reported to introduce the activation of initiation and propagation in the anionic polymerization of alkylene oxides with *t*-BuOK. The presence of a crown ether, 18-crown-6, in the cyclopolymerization allowed the M_n of the polymer to approach the value estimated from the [**1**]/[*t*-BuOK] molar ratio. The complexing agent promoted the dissociation of *t*-BuOK to an initiating anion.

3.2.2 Anionic polymerization of 1,2;5,6-dianhydro-3,4-O-isopropylidene-D-mannitol

Table 3.2 summarizes the results of the polymerization of 1,2;5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol (**3**) using *t*-BuOK. Monomer **3** tended to form a gel in the polymerization process, so that soluble polymers were isolated only at early stages of the polymerization. Such a polymer was powdery and soluble in toluene, chloroform, tetrahydrofuran, and methanol, but insoluble in *n*-hexane. The restriction of free rotation at the C3 and C4-positions of the monomer strongly decreases in its tendency to undergo cyclization.

Table 3.2. Anionic polymerization of 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol (3) using *t*-BuOK[a].

Solvent	Time (h)	Yield (%)	M_n [b]	M_w/M_n [b]	DP_n	f_c [c]	$[\alpha]_{546}^{23}$ [d]
Benzene	2	21.4	3560	2.19	19.1	0.65	+20.3
Benzene	24	gel	-	-			-
THF	3	22.9	8210	2.62	44.1	0.65	+16.0
THF	24	gel		-			-

[a] [**3**]=1.0 mol•L^{-1}; [**3**]/[catalyst]=20; temp, 60℃. [b] Measured in THF by GPC using PSt as the standard. [c] Mole fraction of the cyclic structure units in the polymer. [d] *c* 1.0 in chloroform.

The Vandenberg catalyst system, $2AlEt_3/H_2O$/acetylacetone[1] in toluene, was suitable for the cyclopolymerization of α,β-diepoxides leading to polymeric crown ethers.[2] In the systems for **1** and **3**, no polymer was obtainable. Other coordinate catalytic systems such as $ZnEt_2/H_2O$[3] and $ZnEt_2/CH_3OH$[3] yielded only a trace of oligomers.

3.2.3 Anionic polymerization of 1,2:5,6-dianhydro-3,4-di-O-pentyl-D-mannitol and 1,2:5,6-dianhydro-3,4-di-O-decyl-D-mannitol

Table 3.3 lists the results of the polymerizations of 1,2:5,6-dianhydro-3,4-di-*O*-pentyl-D-mannitol **4** and 1,2:5,6-dianhydro-3,4-di-*O*-decyl-D-mannitol **5** using *t*-BuOK. The catalyst gradually dissolved into the reaction system during a few hours. The solubilities of the resulting polymers in organic solvents were similar to those of the polymers using BF_3•OEt_2. The yield and M_n of the polymers were higher than those using BF_3•OEt_2. The highest value of M_n was 7600 (DP_n = 26.5) for the polymer from **4** in THF and 8400 (DP_n = 19.7) for that from **5** in $C_6H_5CH_3$. The M_w/M_n of the polymers prepared from **4** and **5** was about 1.3. The specific rotations ($[\alpha]_{546}$) were +38.9 and +32.8 for the polymers from **4** and +22.1 and +23.7 for those from **5** (*c*1.0 in $CHCl_3$ at 22 °C).

Table 3.3. Anionic polymerizations of 1,2:3,4-dianhydro-3,4-di-*O*-pentyl-D-mannitol (4) and 1,2:3,4-dianhydro-3,4-di-*O*-decyl-D-mannitol (5)[a]

Monomer	Solvent	Yield (%)	M_n	M_w/M_n[b]	DP_n	$[\alpha]^{22}_{546}$[c]
4	1,4-Dioxane	38.9	6700	1.27	23.4	+38.9
	THF	39.8	7600	1.32	26.5	+32.8
5	$C_6H_5CH_3$	74.7	8400	1.33	19.7	+22.1
	THF	53.4	7600	1.25	17.8	+23.7

[a] Catalyst, *t*-BuOK; [Monomer] = 1.0 mol•L^{-1}; [Monomer]/[*t*-BuOK] = 20; temp, 60 ℃; time, 48 h. [b] Estimated by GPC using polystyrene as standard. [c] *c* 1.0 in $CHCl_3$.

3.3 Discussion

3.3.1 Polymer structure

1,2:5,6-Diepoxyhexane and 1,2-bis(epoxyethyl)benzene capable of forming 5- or 6-membered rings were polymerized to form polymers consisting of tetrahydropyran or tetrahydrofuran recurring units, depending upon the conditions.[4-6] The cationic cyclopolymerization of **1** mainly formed 5-membered rings, (1→6)-bonded 2,5-anhydro-D-glucitol units. Figures 3.1

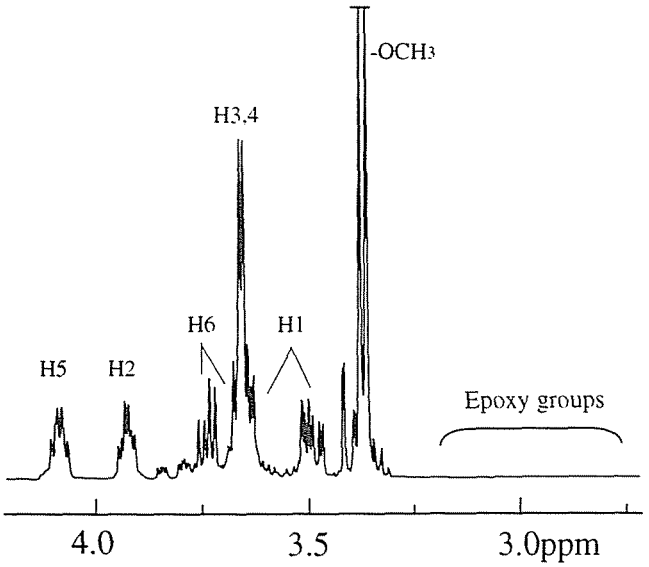


Figure 3.1. ^{1}H NMR spectrum of the polymer prepared from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) using *t*-BuOK in tolutene.

and 3.2 show the ^{1}H and ^{13}C NMR spectra of the polymer prepared by the anionic polymerization of **1**, respectively. Because the characteristic absorption due to the epoxy protons (2.5~3.3 ppm) and carbons (50.02 and 46.51 ppm) completely disappeared and the polymer was soluble in common organic solvents, the polymerization proceeded according to a cyclopolymerization mechanism leading to polymers consisting of cyclic constitutional repeating units, i.e., the extent of cyclization is 100%, whichever initiator may be used.

Figures 3.2 (a) and (b) show the ^{13}C NMR spectra of the polymers

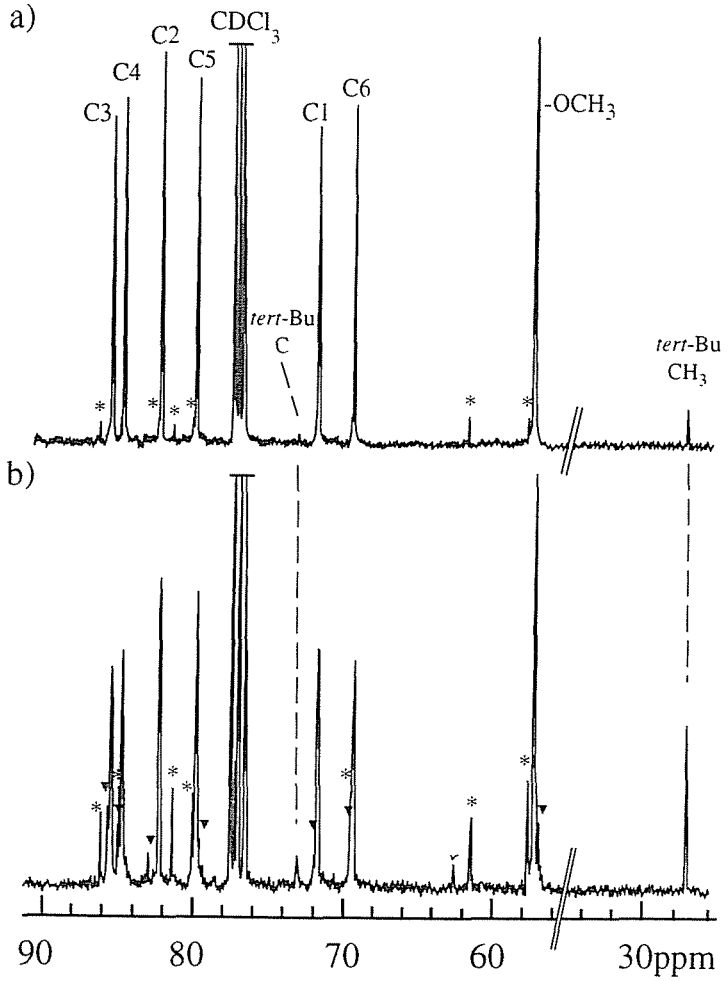
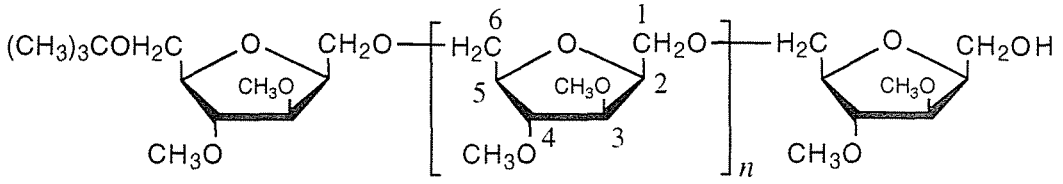


Figure 3.2. ^{13}C NMR spectra of the polymers prepared from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) using *t*-BuOK in tolutene. (a): [**1**]/[*t*-BuOK] = 20; time, 48 hours; M_n = 6410; M_w/M_n = 1.53, (b): [**1**]/[*t*-BuOK] = 5; time, 48 hours; M_n = 1590; M_w/M_n = 1.27. Signals marked with asterisks and solid triangles correspond to the carbons for terminal end unit and initiating end unit, respectively.

obtained at the [**1**]/[*t*-BuOK] ratio of 20 and 5, respectively. The former spectrum contained eight major signals and eight minor ones. In latter spectrum, eight more signals were added to the minor ones. Because their intensity decreased with increasing M_n of the polymer, the minor signals should be due to the two end units in the chain. Table 3.4 compares the major and minor signals with those of 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol (**14**) and 2,5-anhydro-3,4,6-tri-*O*-methyl-D-glucitol (**23**) in the ^{13}C NMR chemical shift. The major signals very closely agreed with **14** corresponding to the constitutional unit in the polymer prepared by cationic polymerization. The minor signals asterisked in Figure 3.2(a) exactly agreed with those in **23**, thus being attributable to a terminal end. Signals at 27.48 and 73.04 ppm belonging to the minor ones are assigned to the methyl carbon and the quaternary carbon in the *tert*-butoxy group being an initiating end, respectively. Each of the additional minor signals marked with the solid triangles in Figure 3.2(b) were slightly shifted from the corresponding major signals. The additional signals, therefore, are attributable to the first cyclic unit bonding to the *tert*-butoxy group.

Moreover, in order to confirm the stereochemistry, the ^{13}C NMR spectrum of the polymer obtained by *t*-BuOK was compared with those of 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-mannitol (**26**) and L-iditol (**27**), being the stereoisomers of **14**. The configurations of the asymmetric carbons at the C2 and C5 positions are *S,S* in **26** and *R,R* in **27**, contrary to *S,R* in **14**. The characteristic resonance at 81.30 and 86.70 ppm due to C2 and C3 for **26** and at 78.53 and 83.29 ppm for **27** were not found in the spectrum of the polymer. Conclusively, the anionic cyclopolymerization of **1** is highly stereoselective and produces a polymer consisting of a stereochemically controlled repeating unit. The polymer molecule is pictured in Chart 3.2. The polymer is (1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol (**25a**) having hydroxymethyl and *tert*-butoxy groups at each of the chain ends.

Chart 3.2



25a

Figures 3.3(a) and (b) show the ^{1}H and ^{13}C NMR spectra of polymer **25d** prepared from **3**. Broadening of these spectra is reflected from the indistinct structure. The signals at 2.6~3.0 ppm in Figure 3.3(a) indicate the presence of unreacted epoxy groups in the polymer. The extent of cyclization was about 65 % which was estimated from the relative areas of the two regions at 2.6~3.0 ppm and at 1.1~1.7 ppm due to the isopropylidene group. This group bonding to the C3 and C4 positions restricted the free rotation around the C-C bond, thus inducing a decreased tendency to undergo cyclization. The structure of cyclic units in the polymer is obscure in the NMR study.

The ^{13}C NMR spectra of the polymers from **4** and **5** using *t*-BuOK are shown in Figure 3.4. For the spectra, the signals due to four methine and two methylene carbons for polymer **25b** from **4** are very close to those for the polymer **25c** from **5**. Both of the signals due to the methine and methylene carbons for these polymers are also close to those for polymer **25a** from **1**. This result indicates that the polymers consist of the 2,5-anhydro-D-mannitol unit. On the other hand, the spectra of the polymers obtained from **4** and **5** using *t*-BuOK were apparently sharper than those of the polymer using $BF_3 \cdot OEt_2$. This result means that the polymerization using *t*-BuOK was more regio- and stereoselective than that using $BF_3 \cdot OEt_2$. Therefore, the structures of the polymers from **4** and **5** using *t*-BuOK were (1→6)-2,5-anhydro-3,4-*O*-pentyl-D-glucitol (**25b**) and (1→6)-2,5-anhydro-3,4-*O*-decyl-D-glucitol (**25c**), respectively.

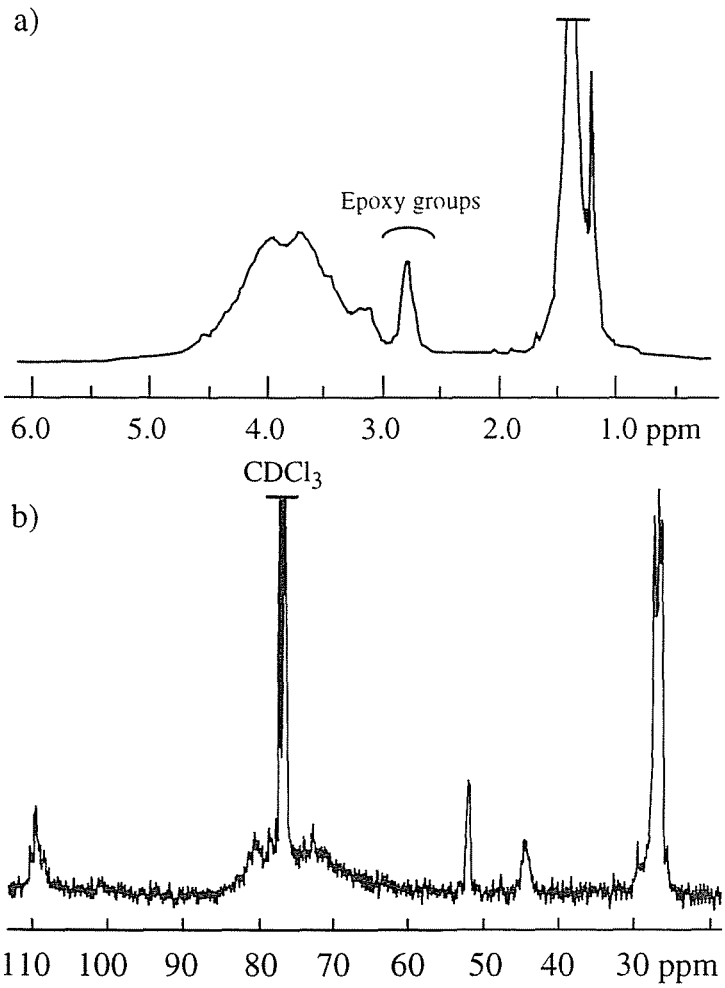


Figure 3.3. ^{1}H (a) and ^{13}C (b) NMR spectra of the polymer prepared from 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol (**3**) using *t*-BuOK in THF: [**3**]/[*t*-BuOK] = 20; time, 3 hours; M_n = 8210; M_w/M_n = 2.62.

For the cyclopolymerization of 3,4-substituted 1,2:5,6-dianhydro-D-mannitols, there was a little difference in the cyclic structural units between the polymers using cationic and anionic catalysts. The stereoregularity in the polymer depended on the catalyst used; nevertheless, the D-mannitol structure in the monomers dominantly changed to the D-glucitol one in the polymers. For the polymerization of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitols, the monomers were regio- and stereoselectively cyclopolymerized to yield (1→6)-3,4-*O*-alkyl-2,5-anhydro-D-glucitols except for the monomer with a 3,4-*O*-isopropylidene group.

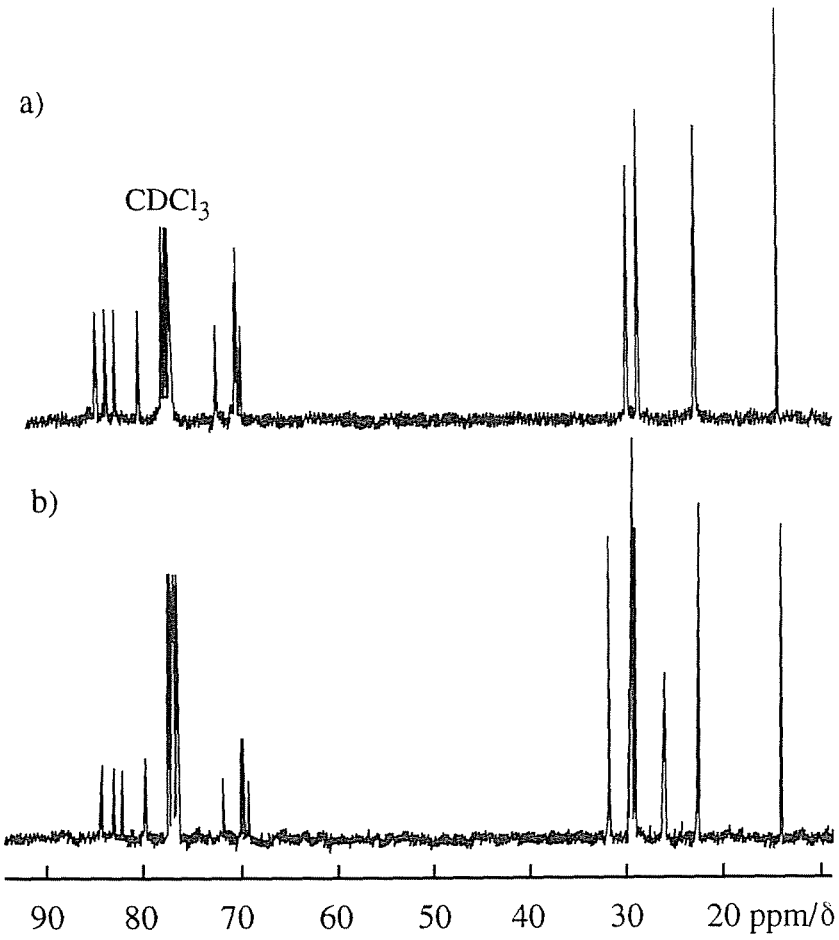
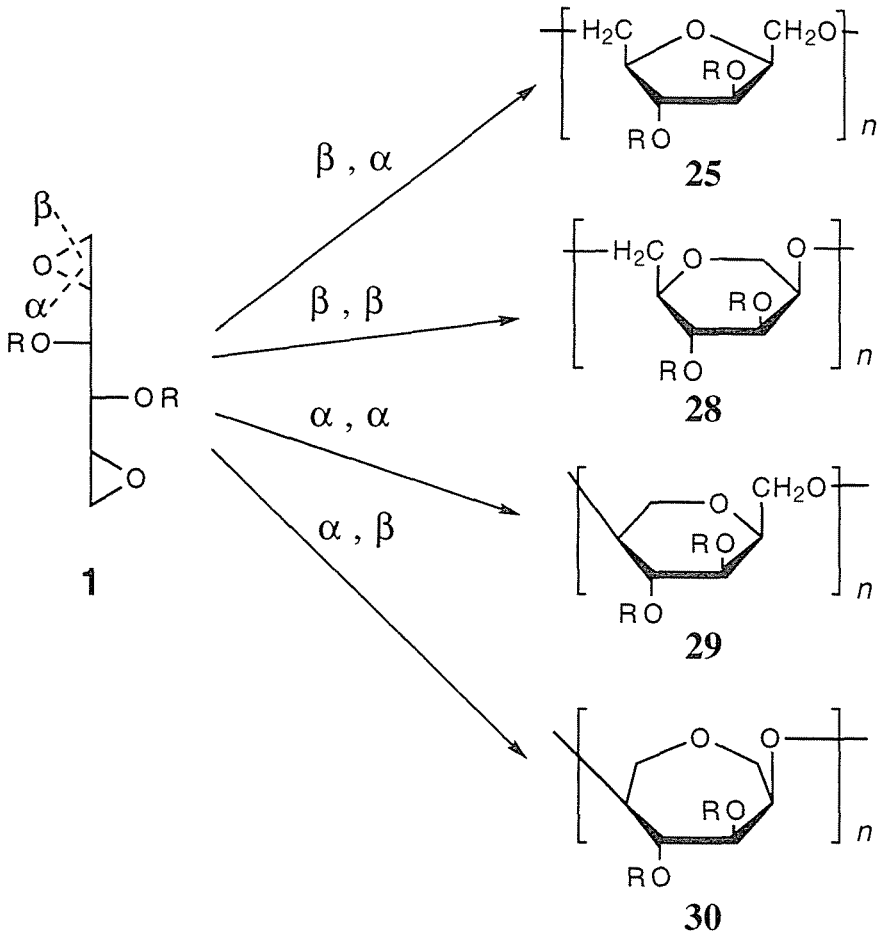


Figure 3.4. ^{13}C NMR sprctra of the polymers prepared from (a) 1,2:5,6-dianhydro-3,4-di-*O*-pentyl-D-mannitol (**4**) and (b) 1,2:5,6-dianhydro-3,4-di-*O*-decyl-D-mannitol (**5**) using *t*-BuOK.

3.3.2 Cyclopolymerization mechanism

Ring opening of mono-substituted epoxides occurs in two ways, i.e., by α- or β-scission. In general, the polymerization using an anionic catalyst (ROK) cleaves predominantly the CH_2-O bond (β-scission) via S_N2 displacement to form the regular head-to-tail linkage.[7] In the anionic cyclopolymerization of 1,2:5,6-dianhydro-D-mannitols, the possible cyclic units by combination of the inter- and intramolecular reactions via the S_N2 reaction are four as shown in Scheme 3.2. β,β- or α,α-Scissions of the two epoxides in a molecule form 6-membered rings (**28** and **29**), whereas β,α- and α,β-scissions lead to the formation of 5- and 7-membered rings (**25** and **30**), respectively.

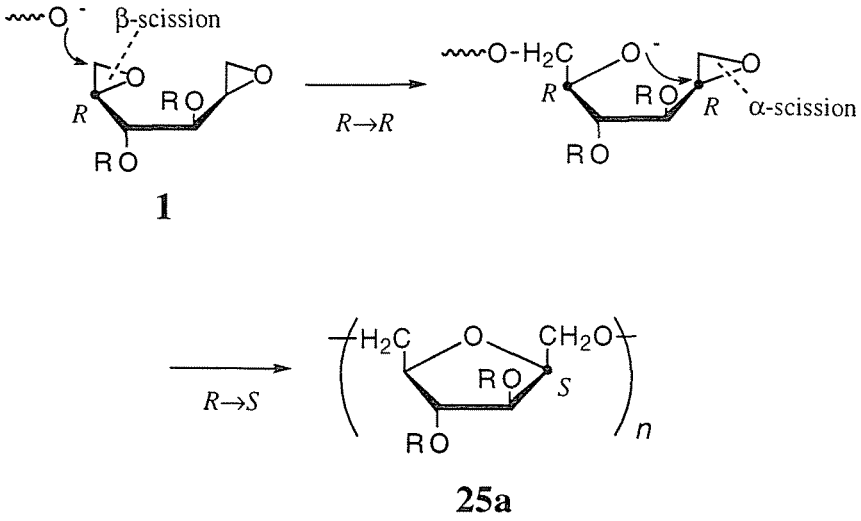
Scheme 3.2[a]



[a] The former and latter symbols correspond to the intermolecular and intramolecular scissions, respectively.

Because the polymers obtained from 1,2:5,6-dianhydro-D-mannitols using anionic catalysts consists of (1→6)-linked 2,5-anhydro-D-glucitol repeating units (**25**), the anionic cyclopolymerization of 1,2:5,6-dianhydro-D-mannitols proceeded through the mechanism with β,α-scissions as shown in Scheme 3.3. For the intermolecular reaction, the growing alkoxy anion attacked the β-carbon of the first epoxide. On the other hand, for the intramolecular cyclization, the alkoxy anion produced from the first epoxide cleaved the α-bond of the second epoxide to form a 5-membered ring.

Scheme 3.3

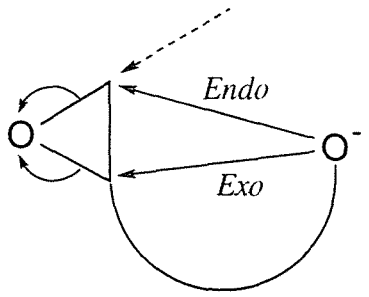


1

25a

It is noteworthy that the attack in the intramolecular reaction occurs, not at the β-carbon, but at the α-carbon. The cyclization along with α-scission is contrary to the usual anionic ring opening of mono-substituted epoxides with β-scission. The regioselectivity in the cyclization, however, can be explained by the Baldwin's rule which is applicable to ring closure on the basis of a stereoelectronic effect in general.[8] The rule clarifies that the cyclization process accompanying the ring opening of a 3-membered ring prefers to form of a 5-membered ring via an *Exo* reaction rather than a 6-membered ring via an *Endo* reaction. In such a case, the positioning of the alkoxy ion along the broken line representing collinear approach requires considerable bond distortion, as shown in Scheme 3.4. Hence the occurrence of α-scission is suitable for intramolecular reaction in the anionic polymerization of 1,2:5,6-dianhydro-D-mannitols. The α-scission inverts the configuration from *R* to *S* in the carbon at the C2 position. The β-scission in the intermolecular reaction retains the *R* configuration in the carbon at the C5 position. Thus, the polymer with only the D-glucitol unit as the constitutional unit is formed from monomers **1**, **4** and **5** being D-mannitol derivatives, and the anionic cyclopolymerization is highly regio- and stereoselective in comparison with the cationic polymerization.

Scheme 3.4



3.4 Conclusions

The anionic cyclopolymerization of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol using potassium *tert*-butoxide and potassium hydroxide was higher regio- and stereoselective than that using cationic catalysts and produced a well-defined polymer, that is, (1→6)-3,4-di-*O*-alkyl-2,5-anhydro-D-glucitol, which has hydroxymethyl and *tert*-butoxy groups at each of the chain ends. For the polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol **1**, the polymer yields and molecular weights were affected both by the monomer to catalyst molar ratio and the polymerization time. The presence of a crown ether, 18-crown-6, in the cyclopolymerization allowed the M_n of the polymer to approach the value estimated from the [**1**]/[*t*-BuOK] molar ratio. On the other hand, 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol tended to form a gel in the polymerization process. The restriction of free rotation at the C3 and C4-positions of the monomer strongly decreased in its tendency to undergo cyclization. The highly selective cyclopolymerization of 1,2:5,6-dianhydro-D-mannitol using the anionic catalyst is a new synthetic method for preparing an artificial polysaccharide.

3.5 Experimental Section

Measurement. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-A400 II and JEOL JNM-EX 270 spectrometers using chloroform-d ($CDCl_3$) with tetramethylsilane as an internal standard. The absorptions in the ^{1}H and ^{13}C NMR spectra of the polymer were assigned on the basis of the results with two-dimensional NMR measurements such as COSY and H-C COSY. Optical rotation measurements were carried out in chloroform solutions using a Jasco DIP-140 digital polarimeter. The molecular weights of the polymers were measured by gel permeation chromatography (GPC) in tetrahydrofuran on a Jasco HPLC system equipped with three polystyrene gel columns (Shodex KF-804L). The number-average molecular weight (M_n) and molecular weight distribution (M_w/M_n) of the polymers were calculated on the basis of polystyrene calibration. In order to confirm the reliability of these M_ns, an additional measurement was carried out using FD-mass spectrometry. The values (M_ns = 1150 and 1680) determined using FD-MS were fortunately similar to those using GPC (M_ns = 1100 and 1590). FD and FI-MS were obtained with a JEOL JMS-SX102A mass spectrometer.

Materials. Potassium *tert*-butoxide (*t*-BuOK) was purified by sublimation of the commercial product under reduced pressure. Potassium hydroxide (KOH) was purified by the following method: 2 g of KOH was dissolved in 20 mL of pure ethanol, and the solution was filtered under nitrogen gas. The solution was concentrated under vacuum using mild heating and then dried under vacuum at 50 °C for 30 h. Tetrahydrofuran, 1,4-dioxane, benzene and toluene were purified by the usual methods and distilled from sodium-benzophenone. 18-Crown-6 was purified by recrystallization from acetonitrile. 1,2;5,6-Dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) was prepared from D-mannitol according to the method of Kuszmann.[9] The method of Merrer et al. was used to synthesize 1,2;5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol

(**3**).[10] Monomers **4** and **5** was synthesized from D-mannitol as described in Chapter 2. Monomers **1**, **3**, **4** and **5** were distilled over CaH_2 under reduced pressure before polymerization run. 2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol (**14**) and 2,5-anhydro-3,4,6-tri-*O*-methyl-D-glucitol (**23**) were synthesized from **1** as described in Chapter 2.

2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-D-mannitol (26). Compound **26** was prepared by methylation of 2,5-anhydro-D-mannitol purchased from Aldrich. To a stirred solution of 2,5-anhydro-D-mannitol (40 mg, 0.244 mmol) in dimethyl sulfoxide (0.3 mL) was simultaneously added a solution of sodium hydroxide (0.11 g, 2.75 mmol) in water (0.11 mL) and dimethyl sulfate (0.12 mL, 1.27 mmol) at a rate that the temperature of 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 the residue purified by thin-layer chromatography with hexane/ethyl acetate (1/1, R_f 0.47) to give pure **26** as a colorless syrup (31 mg, 57.8 %): $[\alpha]_D$ +36.3°, $[\alpha]_{577}$ +38.3°, $[\alpha]_{546}$ +44.1°, $[\alpha]_{435}$ +75.0°, and $[\alpha]_{405}$ +89.0° (*c* 1.0 in $CHCl_3$ at 23 °C); ^{1}H NMR (270MHz, $CDCl_3$): δ 4.10 (ddd, *J* = 9.1Hz, *J*= 5.6Hz, *J*= 1.3 Hz, H2,5, 2H), 3.74 (dd, *J* = 3.4Hz, *J* = 1.3 Hz, H3,4, 2H), 3.51 (dd, *J*= 5.6Hz, *J*= 1.3 Hz, H1,6, 4H), and 3.41 ppm (s, 4MeO ,12H); ^{13}C NMR (68MHz, $CDCl_3$): δ 86.70 (C3,4), 81.30 (C2,5), 72.78 (C1,6), 59.21 (2MeO), and 57.52 ppm (2MeO). Anal. Calcd for $C_{10}H_{20}O_5$: C, 54.53%; H, 9.15%. Found C, 54.28%; H, 9.10%.

2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-L-iditol (27). Compound **27** was synthesized from 2,5-anhydro-L-iditol which was prepared according to the method of Bock et al.[11] 2,5-Anhydro-L-iditol (40 mg, 0.244 mmol) in dimethyl sulfoxide (0.3 mL) was treated with a solution of sodium hydroxide (0.11 g, 2.75 mmol) in water (0.11 mL) and dimethyl sulfate (0.12 mL, 1.27 mmol) as described for **26**, to give, after thin-layer chromatography with hexane/ethyl acetate (1/1, R_f 0.45), pure **7** as a colorless syrup (37.3 mg,

69.6 %): $[\alpha]_D$ +7.1°, $[\alpha]_{577}$ +7.2°, $[\alpha]_{546}$ +8.6°, $[\alpha]_{435}$ +17.9°, and $[\alpha]_{405}$ +22.6° (*c* 1.0 in $CHCl_3$ at 23 °C); ^{1}H NMR (270MHz, $CDCl_3$): δ 4.26~4.20 (m, H2,5, 2H), 3.80(dd, *J*=5.0Hz, *J*= 1.3 Hz, H3,4, 2H), 3.55 (dd, *J*= 6.1Hz, *J*= 4.1 Hz, H-1,6, 4H), 3.41 (s, 2MeO, 6H), and 3.38 ppm (s, 2MeO, 6H); ^{13}C NMR (68MHz, $CDCl_3$): δ 83.29 (C3,4), 78.53 (C2,5), 70.71 (C1,6), 59.14 (2MeO), and 58.03 ppm (2MeO). Anal. Calcd. for $C_{10}H_{20}O_5$: C, 54.53%; H, 9.15%. Found C, 54.91%; H, 8.77%.

Polymerization. All the polymerizations of **1**, **3**, **4** and **5** were carried out in dry benzene, toluene, tetrahydrofuran, and 1,4-dioxane in an H-shaped glass ampule. A typical polymerization procedure is as follows: monomer **1** (0.862 g, 4.95mmol) was added to the one side of the ampoule, and *t*-BuOK (110 mg, 0.986 mmol) and dry toluene (4.95 ml) were added to the other side of the ampoule under a nitrogen atmosphere. After sealing, the monomer and the catalyst solution were mixed at 60°C. After 48 h, the reaction mixture was poured into a large amount of methanol, and the solution was neutralized with diluted hydrochloric acid. After evaporating the solvent, the residue was purified by reprecipitation from chloroform-*n*-hexane to yield the polymer in 96.5 % (0.83 g). The M_n and M_w/M_n were 1590 and 1.27, respectively: $[\alpha]_D$ +64.7°, $[\alpha]_{577}$ +67.6°, $[\alpha]_{546}$ +76.2°, $[\alpha]_{435}$ +125.6°, and $[\alpha]_{405}$ +147.5° (*c* 1.0 in $CHCl_3$ at 23 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.09 (td, *J*= 5.6 Hz, *J*= 4.2 Hz, H5, 1H), 3.93 (td, *J*= 6.0 Hz, *J*= 2.9 Hz, H2, 1H), 3.74 (dd, *J*= 10.2 Hz and *J*= 5.4 Hz, H6, 1H), 3.62~3.69 (m, H3, H4, H1, and H6, each 1H total 4H), 3.46~3.52 (m, H1, 1H), 3.38 (s, CH_3O, 3H), 3.36 (s, CH_3O, 3H), and 1.19 ppm (s, *t*-butoxy); ^{13}C NMR (100 MHz, $CDCl_3$): δ 86.10 (CH), 85.55 (CH), 85.42 (C3), 84.97 (CH), 84.86 (CH), 84.70 (C4), 82.94 (CH), 82.23 (C2), 81.39 (CH), 80.04 (CH), 79.84 (C5), 79.70 (CH), 73.04 (C, *t*-BuO), 71.92 (CH_2), 71.70 (C1), 69.44 (CH_2), 69.38 (CH_2), 69.31 (C6), 61.46 (CH_2), 57.68 (CH_3), 57.34 (CH_3O), 57.27 (CH_3O), 57.09 (CH_3) and 27.48 ppm (CH_3, *t*-BuO).

The polymerization of **3** (407 mg, 2.20 mmol) was carried out by the

above procedure to obtain 87 mg (21.4 % yield) of the polymer with an M_n of 3560 and M_w/M_n of 2.19: $[\alpha]_D$ +17.2°, $[\alpha]_{577}$ +17.3°, $[\alpha]_{546}$ +20.3°, $[\alpha]_{435}$ +32.1°, and $[\alpha]_{405}$ +36.0° (*c* 1.0 in $CHCl_3$ at 23 °C).

The polymerization of **4** in THF using *t*-BuOK gave 199 mg (39.8 % yield) of the polymer. The M_n and M_w/M_n were 7600 and 1.32, respectively. $[\alpha]_{546}$ +32.8° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR ($CDCl_3$) δ 14.02 (CH_3), 22.46, 22.50 (-$\underline{C}H_2CH_3$), 28.33, 28.37 (-OC_2H_4-$\underline{C}H_2$-C_2H_5), 29.48, 29.54 (-$OCH_2\underline{C}H_2$-C_3H_7), 69.39 (C6) 69.77, 69.89 (-OCH_2), 71.96 (C1), 79.97 (C5), 82.44 (C2), 83.26 (C4), and 84.38 ppm (C3).

The polymerization of **5** in THF using *t*-BuOK gave 170 mg (53.4 % yield) of the polymer. The M_n and M_w/M_n were 7600 and 1.25, respectively. $[\alpha]_D$ +23.7° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR ($CDCl_3$) δ 14.11 (CH_3), 22.68 (-$\underline{C}H_2CH_3$), 26.19, 26.24 (CH_2), 29.36(CH_2), 29.54 (CH_2), 29.63, 29.66 (CH_2), 29.84 (CH_2), 29.92 (CH_2), 31.91(CH_2), 69.30 (C6) 69.80, 69.98 (-OCH_2), 72.00 (C1), 79.92 (C5), 82.38 (C2), 83.25 (C4), and 84.45 ppm (C3).

3.6 References

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Regio- and Stereoselective Cyclopolymerization of (2*S*,5*S*)-1,2:5,6-Diepoxyhexane

4.1 Introduction

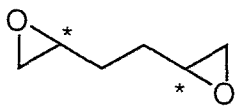
For the cyclopolymerization of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol, the cyclic constitutional units in the resulting polymers depended on the nature of the catalysts used. 3,4-Di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol was cyclopolymerized using $BF_3 \cdot OEt_2$ and $SnCl_4$ to yield polymers consisting mainly of 2,5-anhydro-D-glucitol recurring units along with other cyclic ones. In addition, the polymerization using potassium *tert*-butoxide was highly regio- and stereoselective for producing (1→6)-2,5-anhydro-D-glucitols. The cyclopolymerizability of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol also depended on the character of substituents in 3,4-positions. Therefore, an optically active 1,2:5,6-diepoxyhexane, which corresponds to the substituent-free compound of 1,2:5,6-dianhydro-D-mannitols, is interesting in its cyclopolymerization tendency.

The enantiomeric and diastereomeric mixtures of 1,2:5,6-diepoxyhexane (**(2*SR*,5*RS*)-31**) have been studied with regard to their cyclization and cyclopolymerization.[1-3] Wiggins et al. reported that **(2*SR*,5*RS*)-31** was converted to 2,5-bis(hydroxymethyl)tetrahydrofuran by treatment with boiling water.[1] For the cyclopolymerization of **(2*SR*,5*RS*)-31**, the cyclic repeating units in the resulting polymers were discussed by comparison of the IR and ^{1}H NMR spectra between the polymers and cyclic model compounds. Stille et al. reported that **(2*SR*,5*RS*)-31** was polymerized using cationic and heterogeneous anionic initiators to produce polymers

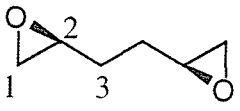
consisting of tetrahydropyran as the cyclic constitutional unit.[2] On the other hand, Bauer reported the polymer consisting of tetrahydrofuran moieties was obtained using a soluble anionic initiator.[3] This ambiguity regarding polymer structure can be clarified using the optically pure isomer of **(2*SR*,5*RS*)-31** and ^{13}C NMR spectral measurements.

In this chapter, the cyclopolymerization of (2*S*,5*S*)-1,2:5,6-diepoxyhexane (**(2*S*,5*S*)-31**) using $BF_3 \cdot OEt_2$ and *t*-BuOK are described. For estimating the cyclization tendency, the methanolysis of **(2*S*,5*S*)-31** is carried out using a catalytic amount of hydrochloric acid. After separating the reaction compounds, (2*R*,5*S*)-2-(hydroxymethyl)-5-(methoxymethyl)tetrahydrofuran (**32**) and (2*R*,5*R*)-2-(hydroxymethyl)-5-methoxytetrahydropyran (**33**) are obtained as the 5- and 6-membered cyclic unimers, respectively. The structures of the cyclic repeating units in the resulting polymers are confirmed by comparing their ^{13}C NMR spectra with those of (2*R*,5*S*)-2,5-bis(methoxymethyl)tetrahydrofuran (**34**) and (2*R*,5*R*)-2-(methoxymethyl)-5-methoxytetrahydropyran (**35**) prepared from the methylation of **32** and **33**, respectively.

Chart 4.1

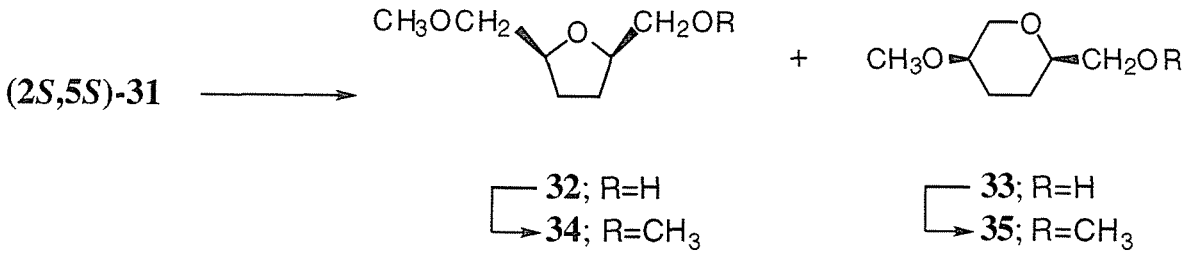


(2*SR*,5*RS*)-31



(2*S*,5*S*)-31

Scheme 4.1



4.2 Results

(2*S*,5*S*)-1,2:5,6-Diepoxyhexane (**(2*S*,5*S*)-31**) was prepared from D-mannitol according to the procedure of Machinaga et al.[4] At room temperature, **(2*S*,5*S*)-31** is colorless liquid. The monomer has a C_2 symmetric property because only three peaks are present in the ^{13}C NMR spectrum of Figure 4.1.

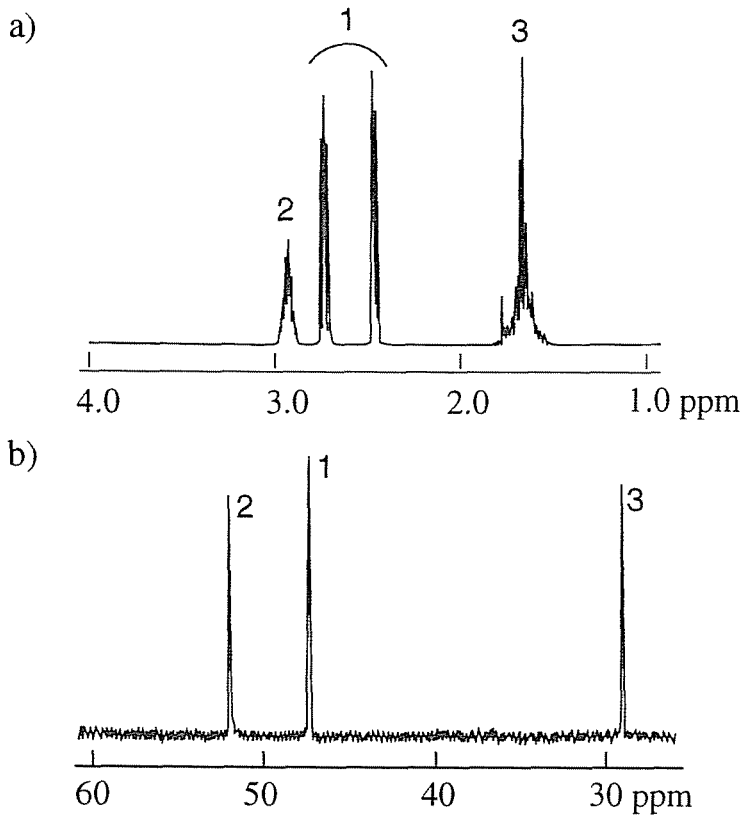


Figure 4.1. ^1H and ^{13}C NMR spectra of (2*S*,5*S*)-1,2:5,6-diepoxyhexane (**(2*S*,5*S*)-31**)

Table 4.1 lists the results of the polymerization of (2*S*,5*S*)-1,2:5,6-diepoxyhexane (**(2*S*, 5*S*)-31**) using BF_3•OEt_2 and *t*-BuOK. After BF_3•OEt_2 was added to the monomer solution with the monomer concentration ([M]) of 0.5 mol•L^{-1}, the polymerization system became immediately heterogeneous. About one half of the resulting polymer was soluble in chloroform and THF, but the

rest was insoluble. On the other hand, the polymerization at the [M] of 0.2 mol•L^{-1} proceeded homogeneously to give the organic solvent-soluble polymer. Number-average molecular weights (M_n) were 1300~3600, corresponding to number-average degree of polymerization (DP_n) of 11.4~31.6. Specific rotations ($[\alpha]^{22}_D$) ranged from +3.0 to +7.2° (*c* 1.0 in $CHCl_3$).

Table 4.1. Cyclopolymerization of (2*S*,5*S*)-1,2:5,6-diepoxyhexane ((2*S*,5*S*)-31) using BF_3•OEt_2 and *t*-BuOK

Catalyst	Solvent	[M] mol•L^{-1}	Yield %	f_c [c]	M_n (M_w/M_n) [d]	$[\alpha]^{22}_D$ [e]
BF_3•OEt_2 [a]	$C_6H_5CH_3$	0.5	47.3[f]	0.72	3600 (4.3)	+3.0
	CH_2Cl_2	0.5	48.6[g]	0.78	3100 (4.9)	+4.2
	CH_2Cl_2	0.2	49.6	0.90	1300 (5.5)	+7.2
t-BuOK[b]	$C_6H_5CH_3$	1.0	87.8	>0.99	6500 (1.8)	-1.6
	1,4-Dioxane	1.0	97.4	>0.99	6300 (1.4)	-1.6

[a] [(2*S*,5*S*)-**1**]/[BF_3•OEt_2]=100; temp., 0℃; time, 48 h. [b] [(2*S*,5*S*)-**31**]/[*t*-BuOK]=25; temp., 60℃; time, 48 h. [c] The mole fraction of cyclized units in the polymer determined by ^{1}H NMR spectrum. [d] Measured in THF by GPC using poly(styrene) as standard. [e] Measured in $CHCl_3$ (*c* 1.0). [f] Organic solvent-insoluble polymer was 31.8 %. [g] Organic solvent-insoluble polymer was 46.3 %.

For the polymerization using *t*-BuOK, the catalyst gradually dissolved into the polymerization system after several hours and the system turned brown. Although the [M] was higher than that using BF_3•OEt_2, the polymerization proceeded homogeneously to give the organic solvent-soluble polymers in high yields. The M_ns of 6300 and 6500, which corresponded to DP_ns of 55.2 and 56.9, respectively, were higher than those using BF_3•OEt_2. The polymers obtained had also higher DP_n than those of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol. The specific rotation ($[\alpha]^{22}_D$) was -1.6° (*c* 1.0 in $CHCl_3$) and its sign was the opposite of that for the polymer using BF_3•OEt_2.

4.3 Discussion

4.3.1 Polymer structure

Figure 4.2 shows the ^{1}H NMR spectra of the polymers obtained using BF_3•OEt_2 and *t*-BuOK. The characteristic absorptions at 2.51 and 2.78 ppm due to the epoxy groups were observed in Figure 4.2(a), so the polymer using BF_3•OEt_2 contained unreacted epoxy groups. The mole fractions of cyclized units (f_c) in the polymer, which was determined from the relative peak areas of the protons in the ^{1}H NMR spectra, were 0.76 ~ 0.90. On the contrary, since the ^{1}H NMR spectra of the polymers using *t*-BuOK in Figure 4.2(b) indicated the absence of the epoxy groups, the polymerization proceeded according to a

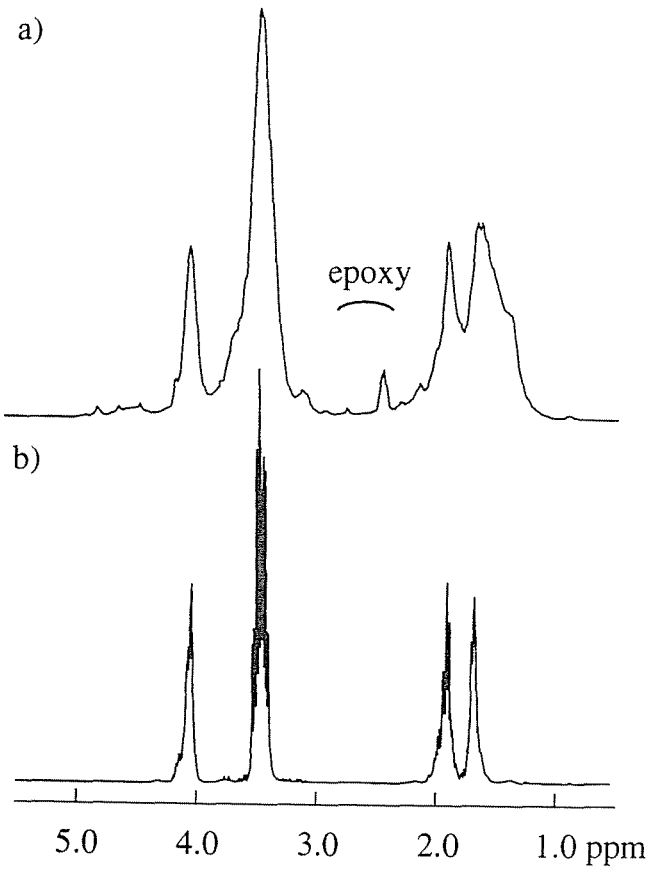


Figure 4.2. ^{1}H NMR spectra of the polymers prepared from (2*S*,5*S*)-1,2:5,6-diepoxyhexane (**(2*S*,5*S*)-31**) using (a) BF_3•OEt_2 in CH_2Cl_2 and (b) *t*-BuOK in toluene.

cyclopolymerization mechanism leading to the polymers consisting of cyclic constitutional repeating units, i.e., the f_c over 0.99.

The ^{13}C NMR spectrum of the polymer obtained using *t*-BuOK showed clearly three signals at 78.40, 74.23, and 27.92 ppm, which were assigned to the CH, OCH_2, and CH_2 carbons, respectively, as shown in Figure 4.3. For the polymer with BF_3•OEt_2, the similar signals marked with the open circles were also observed at 78.37, 74.14, and 27.86 ppm. In addition, there are multiple small absorptions along with the signal at 43.83 ppm due to the residual epoxy carbon.

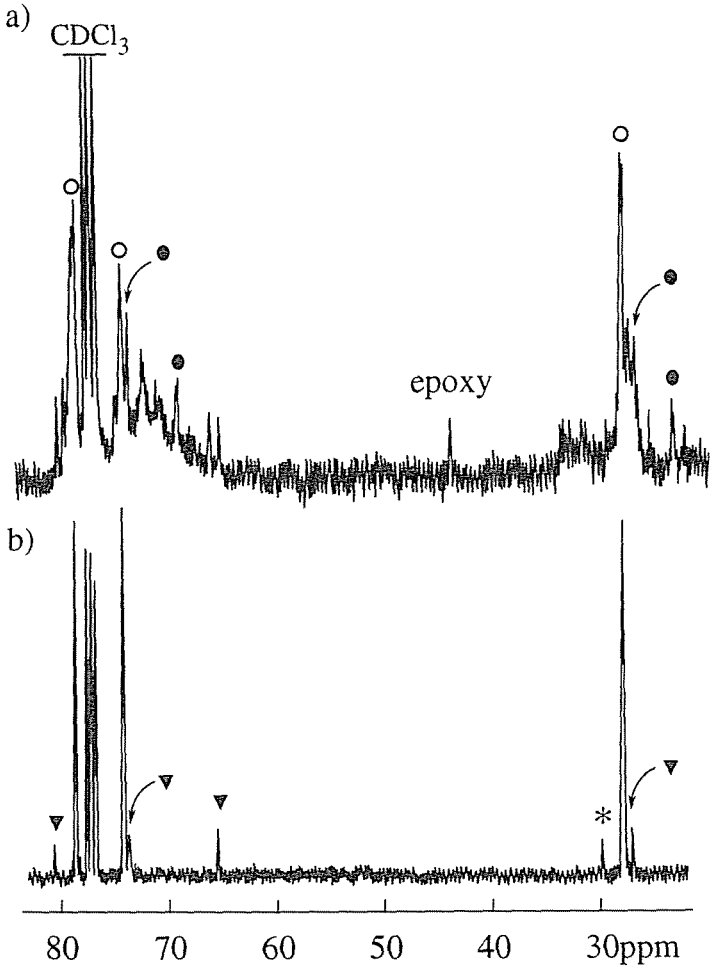


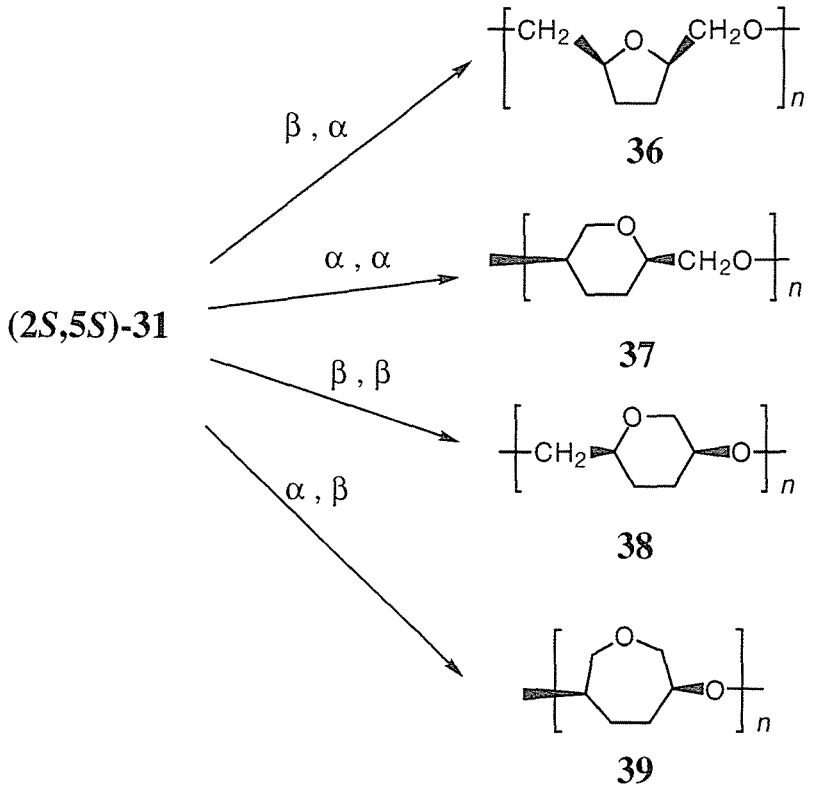
Figure 4.3. ^{13}C NMR spectra of the polymers prepared from (2*S*,5*S*)-1,2:5,6-diepoxyhexane (**(2*S*,5*S*)-31**) using (a) BF_3•OEt_2 in CH_2Cl_2 and (b) *t*-BuOK in toluene.

These NMR spectral measurement results indicate that the polymer structure obtained using *t*-BuOK was highly regio- and stereoselective, while that using BF_3•OEt_2 was irregular. This was very similar to the cyclopolymerization tendency of 3,4-di-*O*-alkyl-1,2:5,6-diahhydro-D-mannitol.

4.3.2 Cyclopolymerization mechanism

For the cationic polymerization of monosubstituted epoxides through an S_N2-type mechanism, the configuration of the asymmetric carbon atom is inverted due to the ring-opening at the CH-O bond (α-scission) and retained by the ring-opening of the CH_2-O bond (β-scission).[5] On the other hand, the anionic polymerization exclusively proceeds through β-scission.[5] For the

Scheme 4.2[a]

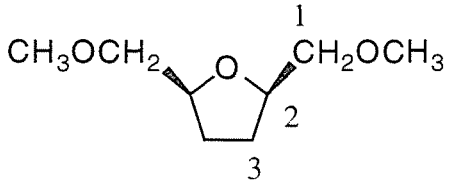


[a] The former and latter symbols correspond to the intermolecular and intramolecular scissions, respectively.

polymerization of (**2*S*,5*S*)-31**, Scheme 4.2 represents the possible cyclic units. The intermolecular cyclization and the intramolecular reaction through α,α- and β,β-scissions of the two epoxides in a monomer molecule form the 6-membered rings **37** and **38**, respectively, whereas β,α- and α,β-scissions lead to the formation of the 5- and 7-membered rings **36** and **39**, respectively.

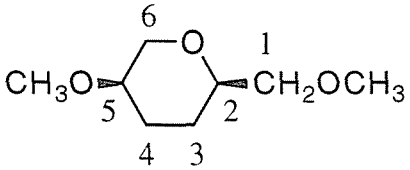
In order to estimate the cyclization tendency using a cationic catalyst, **(2*S*,5*S*)-31** was reacted in MeOH using a catalytic amount of hydrochloric acid. (2*R*,5*S*)-2-(Hydroxymethyl)-5-(methoxymethyl)tetrahydrofuran (**32**) and (2*R*,5*R*)-2-(hydroxymethyl)-5-methoxytetrahydropyran (**33**) were obtained as the cyclic unimers in the ratio of 8/7. In addition, they were methylated to (2*R*,5*S*)-2,5-bis(methoxymethyl)tetrahydrofuran (**34**) and (2*R*,5*R*)-2-(methoxymethyl)-5-methoxytetrahydropyran (**35**) for confirming

Chart 4.2



34

C	δ/ppm
1	75.43
2	78.37
3	27.77
CH_3O	59.23



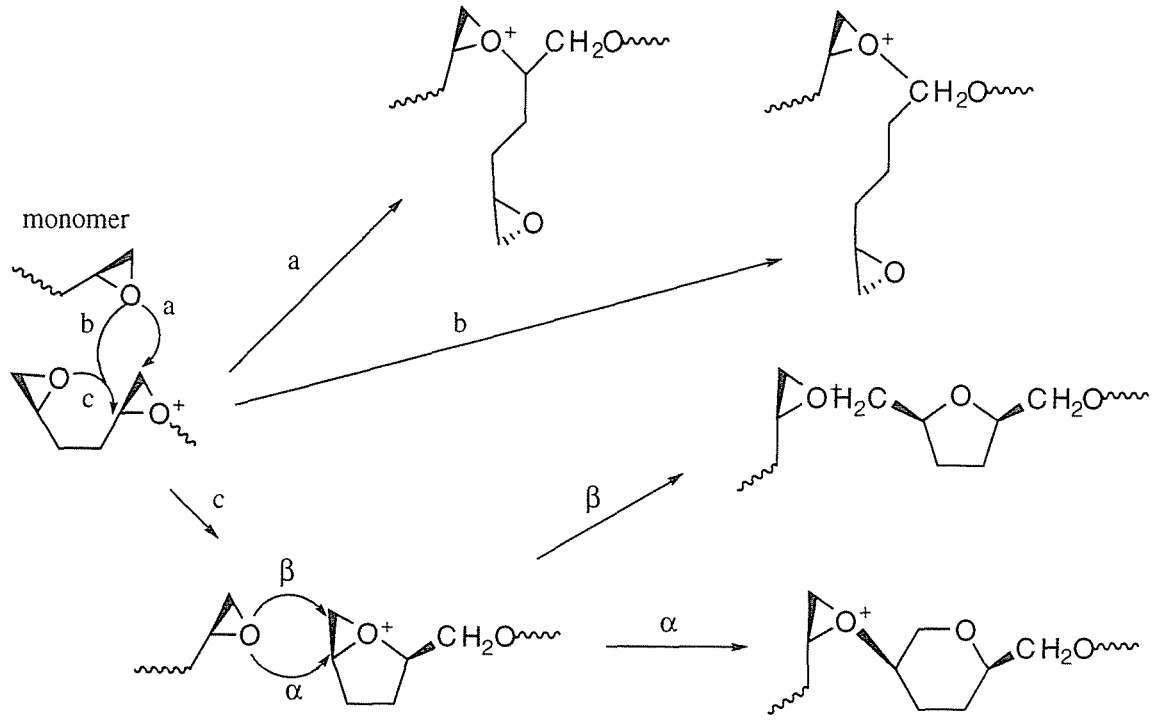
35

C	δ/ppm
1	76.08
2	76.50
3	22.84
4	26.35
5	73.20
6	68.74
CH_3O	56.09
CH_3O	59.18

the cyclic structures in the polymers. The chemical shifts of the ^{13}C NMR signals for **34** and **35** are summarized in Chart 4.2.

The signals at 78.37, 74.14, and 27.86 ppm for the polymer obtained using BF_3•OEt_2 were very close to the chemical shift values of 78.37 (CH), 75.43 (CH_2O), and 27.77 ppm (CH_2) for **34**; therefore, the main cyclic structure was the 5-membered ring **36**. In addition, because the absorptions marked with the solid circles were similar to the chemical shifts for **35**, the 6-membered ring **37** should be contained in the polymer. However, many other smaller signals were observed and their assignments were not clear. The polymer using BF_3•OEt_2 consisted of the 5- and 6-membered rings as cyclic units along with a pendant epoxy group unit. This structural characteristic is consistent with the cationic cyclization tendency of **(2*S*,5*S*)-31** in which the 5- and 6-membered cyclic unimers, **32** and **33**, are simultaneously formed. The results elucidate that the cationic cyclopolymerization of **(2*S*,5*S*)-31** has lower regio- and stereoselectivity than that of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol.

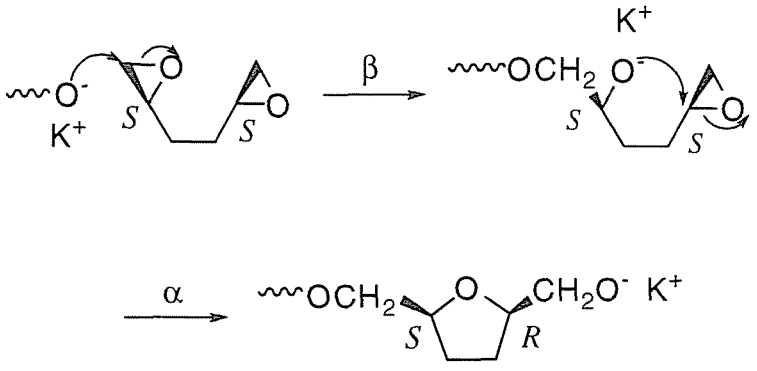
Scheme 4.3



On the other hand, the polymer using *t*-BuOK essentially consisted of the 5-membered cyclic repeating unit, because the signals at 78.40, 74.23, and 27.92 ppm were mainly observed. The small signal marked with an asterisk at 30.28 ppm is assigned to the methyl carbons of the *tert*-butoxy group and those marked with the solid triangles at 80.17, 65.16, 27.74, and 27.18 ppm were very close to the chemical shifts of **32**. This means that the polymer has *tert*-butoxy and hydroxymethyl groups at both ends of the polymer chain. Therefore, the anionic cyclopolymerization of **(2*S*,5*S*)-31** proceeds through a highly regio- and stereoselective mechanism as well as that of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol; i.e., the intermolecular reaction proceeds through the β-scission of the first epoxide and the intramolecular cyclization through the α-scission of the second epoxide to form a 5-membered ring.

For chiroptical property, the sign of the optical rotation for the polymer obtained using $BF_3 \cdot OEt_2$ was opposite to that with *t*-BuOK, which should be caused by the difference in content of major and minor cyclic and acyclic units between both polymers.

Scheme 4.4



4.4 Conclusions

The cyclopolymerizations of **(2*S*,5*S*)-31** using $BF_3 \cdot OEt_2$ and *t*-BuOK were carried out. For the polymer obtained using $BF_3 \cdot OEt_2$, the cyclic constitutional repeating units were the 5- and 6-membered rings together with a pendant epoxy group unit. The polymer using *t*-BuOK essentially consisted of the 5-membered cyclic repeating unit. The cationic cyclopolymerization of **(2*S*,5*S*)-31** has lower regio- and stereoselectivity than that of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol. On the other hand, the anionic cyclopolymerization of **(2*S*,5*S*)-31** proceeds through a highly regio- and stereoselective mechanism as well as that of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol. These results eliminated the ambiguity on the polymer structures for the cationic and anionic cyclopolymerizations of **(2*SR*, 5*RS*)-31**.

4.5 Experimental Section

Measurements. ^{1}H and ^{13}C NMR spectra were recorded using a JEOL JNM-EX270 instrument. Optical rotations were determined using a Jasco DIP-140 digital polarimeter. The molecular weight of the resulting polymers was measured by gel permeation chromatography (GPC) in tetrahydrofuran on a Jasco HPLC system equipped with three polystyrene gel columns (Shodex KF-804L). The number-average molecular weight (M_n) was calculated on the basis of a polystyrene calibration.

Materials. Boron trifluoride etherate ($BF_3 \cdot OEt_2$) was purified by distillation of a commercial product under reduced pressure and used as a solution in dry dichloromethane. Potassium *tert*-butoxide (*t*-BuOK) was purified by sublimation under vacuum before use. Dichloromethane, 1,4-dioxane, and toluene were purified by the usual methods, and dichloromethane was distilled over calcium hydride and 1,4-dioxane and toluene from sodium-benzophenone ketyl.

(2*S*,5*S*)-1,2:5,6-Diepoxyhexane ((2*S*,5*S*)-31) Compound **(2*S*, 5*S*)-31** was prepared by the procedure of Machinaga et al.[4] Bp 98~101 °C /25 mm Hg (lit. bp 76 °C/16 mmHg); $[\alpha]_D$ -23.7° (*c* 1.0, $CHCl_3$) (lit. $[\alpha]_D$ -26.4° (*c* 1.86, $CHCl_3$)); ^{1}H NMR ($CDCl_3$): δ 2.93~3.02 (m, CH, 2H), 2.78 (dd, J = 4.8 Hz, J = 4.1 Hz, CH_2O, 2H), 2.51 (dd, J = 5.0 Hz, J = 2.6 Hz, CH_2O, 2H), and 1.60~1.85 ppm (m, CH_2, 4H); ^{13}C NMR ($CDCl_3$): δ 51.59 (CH), 47.05 (CH_2O), and 28.73 ppm (CH_2).

Cyclopolymerization. The polymerizations using $BF_3 \cdot OEt_2$ and *t*-BuOK were carried out by a procedure similar to that described in Chapter 2 and 3. The anionic polymerization was carried out in toluene using *t*-BuOK; ^{1}H NMR ($CDCl_3$): δ 4.05~4.09 (m), 3.37~3.57 (m), 1.83~2.04 (m), and 1.63~1.78 ppm (m). ^{13}C NMR ($CDCl_3$): δ 78.40 (CH, epoxy), 74.23 (CH_2, epoxy), and 27.92 ppm (CH_2).

Model cyclization. A solution of **(2*S*,5*S*)-31** (1.0 g, 8.76 mmol) in methanol (100 mL) containing a drop of hydrochloric acid was stirred at room temperature for 24 h. The mixture was neutralized by adding methanolic sodium methoxide and then evaporated under reduced pressure. The residue was purified by column chromatography with ethyl acetate/diethyl ether (1/1) to yield (2*R*,5*S*)-2-(hydroxymethyl)-5-(methoxymethyl)tetrahydrofuran (**32**) (0.54 g, 41 %) and (2*R*,5*R*)-2-(hydroxymethyl)-5-methoxytetrahydropyran (**33**) (0.45 g, 34 %). **32**: $[\alpha]_D$ -11.2° (*c* 1.0 $CHCl_3$ at 22°C); ^{1}H NMR ($CDCl_3$): δ 1.75~2.00 (m, CH_2, 4H), 2.80 (s, OH, 1H), 3.35~3.48 (m, $C\underline{H}_2OCH_3$, 2H), 3.40 (s, OCH_3, 3H), 3.53 (dd, *J* = 9.9 Hz, *J* = 3.6 Hz, $C\underline{H}_2OH$, 1H), 3.76 (d, *J* = 11.6 Hz, $C\underline{H}_2OH$, 1H), and 4.05~4.17 ppm (m, CH, 2H); ^{13}C NMR ($CDCl_3$): δ 27.05 (CH_2), 27.94 (CH_2), 59.11 (OCH_3), 65.16 (CH_2OH), 75.11 ($\underline{C}H_2OCH_3$), 78.35 (CH), and 80.15 ppm (CH). Anal. Calcd for $C_7H_{14}O_3$: C,57.51; H, 9.65. Found: C, 57.72; H, 9.37. **33**: $[\alpha]_D$ +17.4° (*c* 1.0, $CHCl_3$ at 22°C); ^{1}H NMR ($CDCl_3$): δ 1.34~1.39 (m, CH_2, 1H), 1.60~1.69 (m, CH_2, 2H), 2.06~2.13 (m, CH_2, 1H), 2.61 (s, OH, 1H), 3.26 (s, CH, 1H), 3.37 (s, OCH_3, 3H), 3.45~3.56 (m, CH, 1H), 3.51 (dd, *J* = 12.4 Hz, *J* = 1.5 Hz, CH_2O, 1H), 3.56~3.59 (m, $C\underline{H}_2OH$, 2H), and 4.07~4.14 ppm (m, CH_2O, 1H); ^{13}C NMR ($CDCl_3$): δ 22.01 (CH_2), 25.81 (CH_2), 56.07 (OCH_3), 65.88 (CH_2OH), 68.92 (CH_2O), 73.22 (CH), and 77.94 ppm (CH). Anal. Calcd for $C_7H_{14}O_3$: C,57.51; H, 9.65. Found: C, 57.14; H, 9.37.

(2*R*,5*S*)-2,5-Bis(methoxymethyl)tetrahydrofuran (34). To a stirred solution of **32** (0.20 g, 1.8 mmol) in 10 mL of dimethyl sulfoxide were simultaneously added a solution of sodium hydroxide (0.30 g, 7.5 mmol) in 0.3 mL of water and dimethyl sulfate (0.50 g, 4.0 mmol) at such a rate that 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 the residue was purified by column chromatography with *n*-hexane/diethyl ether (1/3) to give **34** (77 mg, 35 %): ^{1}H NMR ($CDCl_3$):

δ 1.58~1.74 (m, CH_2, 2H), 1.88~2.03 (m, CH_2, 2H), 3.32~3.45 (m, CH_2O, 4H), 3.38 (s, OCH_3, 6H), and 4.08 ppm (ddd, J = 7.1 Hz, J = 5.1 Hz, J = 2.1 Hz, CH, 2H); ^{13}C NMR ($CDCl_3$): δ 27.77 (CH_2), 59.23 (OCH_3), 75.43 (CH_2O), and 78.37 ppm (CH). Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 59.81; H, 10.01.

(2*R*,5*R*)-2-(Methoxymethyl)-5-methoxytetrahydropyran (35). The synthetic procedure is the same as that for **34** (57 mg, 26 %). $[\alpha]_D$ +40.6° (*c* 1.0, $CHCl_3$ at 22°C); ^1H NMR ($CDCl_3$): δ 1.37~1.45 (m, CH_2, 1H), 1.56~1.72 (m, CH_2, 2H), 2.00~2.14 (m, CH_2, 1H), 3.24~3.64 (m, $C\underline{H}_2OCH_3$, CH, 4H), 3.37 (s, OCH_3, 3H), 3.38 (s, OCH_3, 3H), 3.50 (dd, J = 12.5 and 1.3 Hz, CH_2O, 1H), and 4.25 ppm (ddd, J = 12.4 Hz, J = 4.3 Hz, J = 2.1 Hz, CH_2O, 1H); ^{13}C NMR ($CDCl_3$): δ 22.84 (CH_2), 26.35 (CH_2), 56.09 (OCH_3), 59.18 (OCH_3), 68.74 (OCH_2), 73.20 (CH), 76.08 ($\underline{C}H_2OCH_3$), and 76.50 ppm (CH). Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 59.72; H, 9.33.

4.6 References

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Chapter 5

Cyclopolymerization of 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol to Form (6→1)-2,5-Anhydro-3,4-di-*O*-methyl-D-glucitol

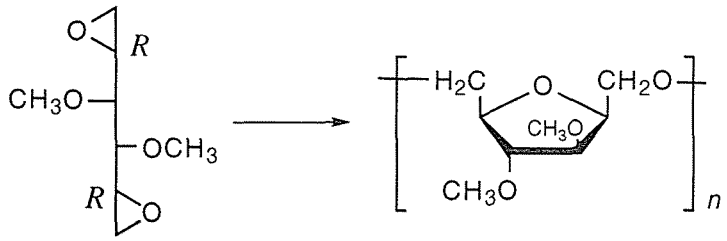
5.1 Introduction

Previous chapters have described that the cationic and anionic cyclopolymerization of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol were controlled through the regio- and stereoselective mechanisms. For the cyclopolymerization, the intermolecular cyclization and the intramolecular reaction proceeded through β,α-scissions of two epoxides in a monomer molecule. The resultant polymers consisted of a (1→6)-linked five-membered constitutional unit, that is, (1→6)-3,4-di-*O*-alkyl-2,5-anhydro-D-glucitol which is a novel polymeric sugar lacking the anomeric linkage.[1-6] The cyclopolymerization presents a new preparative method for polysaccharide. According to the mechanism, the other diastereomer of 1,2:5,6-dianhydro-D-mannitol should also produce the same polymer structure. L-Iditol is a reliable candidate, because it possesses a C_2 symmetric axis as well as D-mannitol but differs from D-mannitol in absolute configuration at the C2 and C5 carbons, i.e., the *S*,*S*-configuration for L-iditol and the *R*,*R*-one for D-mannitol.

In order to obtain further information on the regio- and stereoselective cyclopolymerization of 1,2:5,6-dianhydrohexitol, this chapter describes the cationic and anionic cyclopolymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-L-iditol (**40**), which is a diastereomer of **1** (Scheme 5.1). The structure of the polymer from **40** are confirmed by comparing the ^{13}C NMR spectrum with that of the polymer from **1**. The configurational relationships between the

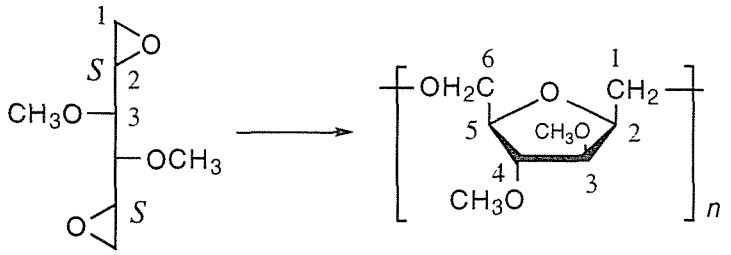
homopolymers obtained from **1** and **40** are also discussed on the basis of the copolymerization between these monomers.

Scheme 5.1



1

10a: using $BF_3 \cdot OEt_2$
25a: using *t*-BuOK



40

41a: using $BF_3 \cdot OEt_2$
41b: using *t*-BuOK

5.2 Results

5.2.1 Cationic polymerization

1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol (**40**) was prepared from D-mannitol according to the reported procedure.[7] Monomer **40** was solid in room temperature, although monomer **1** was white liquid. The ^{13}C NMR spectrum of **40** had only four peaks due to C_2 symmetric property of the monomer (Figure 5.1). The four peaks were due to epoxy carbons at 42.83 and 52.03 ppm, methoxy carbons at 58.64, and methylene carbon at 82.95 ppm.

Table 5.1 lists the results of the cationic polymerization of monomer **40** using $BF_3 \cdot OEt_2$ and $SnCl_4$. The polymerization using $BF_3 \cdot OEt_2$ proceeded

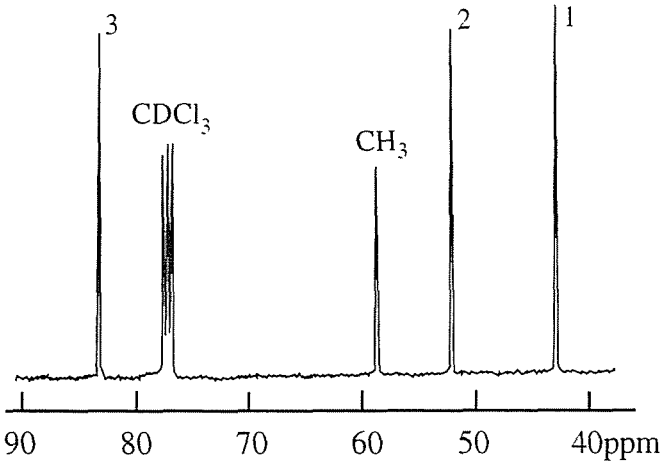


Figure 5.1. ^{13}C NMR spectrum of 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol (**40**).

homogeneously except for that in toluene. The polymers were sticky semi-solid, and their solubility were similar to those of the polymers from **1**. From the reaction system after terminating the polymerization, small amounts of **40** was recovered and the *n*-hexane-soluble, low molecular weight products were also obtained. For all the polymerization conditions, the polymers had lower yields and M_ns than those from **1**. The polymerization in toluene at 0°C proceeded heterogeneously and gave a 12.4% yield of organic solvent-insoluble polymer and a 15.5% of gel-free one, as well as the polymerization of **1**. The M_ns of the polymers obtained at -30 °C were below 1000 and those at 0 °C were 1000~1560 which corresponds to the DP_n of 5.5~9.0.

For the polymerization using $SnCl_4$ for 24 h, the polymer yields were very low, most of the monomers were recovered, and the *n*-hexane-soluble oligomers were not produced. The obtained polymers were sticky semi-solid, and the M_ns were 1430 and 1720.

The cationic polymerizability of **40** differed apparently from that of **1** and the former was inferior to the latter. The specific rotations ($[\alpha]_{546}$) of the polymers were +38.2° ~ +62.9° for **40** (*c* 1.0 in $CHCl_3$ at 22 °C). However, for both polymers, the obvious relation between the specific rotation and the M_n was not observed.

Table 5.1. Cationic polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-L-iditol (40)[a]

Catalyst	Solvent	Temp °C	Yield %	M_n[b]	M_w/M_n[b]	DP_n	$[\alpha]^{22}_{546}$[c]
$BF_3 \cdot OEt_2$	$C_6H_5CH_3$	-30	trace	<1000	1.58		+45.1
	CH_2ClCH_2Cl	-30	5.5	<1000	1.53		+45.1
	CH_2Cl_2	-30	6.1	<1000	2.03		+45.1
	$C_2H_5NO_2$	-30	6.5	<1000	1.33		+44.8
	$C_6H_5CH_3$	0	15.5[d]	1,450	1.54	8.3	+62.9
	CH_2Cl_2	0	45.4	1,430	1.97	8.2	+43.1
	$C_6H_5NO_2$	0	35.7	1,560	1.57	9.0	+52.3
	$C_2H_5NO_2$	0	20.7	<1000	1.28		+42.5
$SnCl_4$	CH_2Cl_2	-30	trace	1,430	1.29	8.2	+42.3
	CH_2Cl_2	0	6.7	1,720	1.81	9.9	+38.2

[a] [**40**]=0.5mol•L^{-1}; [**40**]/[Cat.]=100; time, 24h. [b] Measured in THF by GPC using PSt as standard. [c] Measured in $CHCl_3$ (*c* 1.0). [d] Organic solvent-insoluble polymer was 12.4%.

5.2.2 Anionic polymerization

The anionic polymerization of **40** was carried out using *t*-BuOK and KOH. The typical results are shown in Table 5.2. Both catalysts were effective at relatively high temperatures. The KOH catalyst in toluene was less active than the *t*-BuOK catalyst, due to its lower solubility in the solvent. The polymerization systems were homogeneous up to a very high conversion. The obtained polymers were yellow-brown sticky semisolids which were soluble in chloroform and tetrahydrofuran, and insoluble in *n*-hexane. The polymer had a number-average molecular weight (M_n) ranging from 2600 to 6100 which corresponds to number-average degree of polymerization (DP_n) from 15 to 35.

Table 5.2. Anionic polymerization of 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-idtol (40)[a]

Catalyst	[40]/[Cat.]	solvent	Time h	Yield %	M_n [b]	M_w/M_n [b]	DP_n
t-BuOK	10	Toluene	85	98.5	2560	1.37	14.7
	20	Toluene	85	98.6	3390	1.54	19.5
	20	THF	85	95.0	2950	1.31	17.0
KOH	5	THF	100	92.5	6110	1.60	35.1
	5	Toluene	100	60.4	6000	1.59	34.5

[a] [**40**]=1.0 mol•L^{-1}; temp, 60℃. [b] Measured in THF by GPC using polystyrene as the standard.

5.3 Discussion

5.3.1 Polymer structure

Figure 5.2 shows the ^{1}H NMR spectra of the polymers obtained from **40** using BF_3•OEt_2 and *t*-BuOK. Since the characteristic signals at 3.1~3.3 and 2.8~3.6 ppm due to the epoxy groups completely disappeared, the polymerization proceeded according to a cyclopolymerization mechanism leading to the polymers with cyclic constitutional repeating units, i.e., the extent of cyclization was 100 %. In both spectra, an apparent difference was observed, which reflects the difference in stereochemistry between the polymers from the systems of BF_3•OEt_2 and *t*-BuOK.

Scheme 5.2 represents the possible cyclic units forming through the S_N2-type mechanism. Reactivities of two epoxy groups in **40** are chemically equivalent, because the monomer was a C_2 symmetrical compound. When the polymerizations of **40** proceed through a cyclopolymerization mechanism, as well as monomer **1**, the possible cyclic units of the obtained polymer are four varieties. For the cationic and anionic polymerizations, the α,α- and β,β-scissions lead to the 6-membered rings **43** and **42**, respectively, which fact is

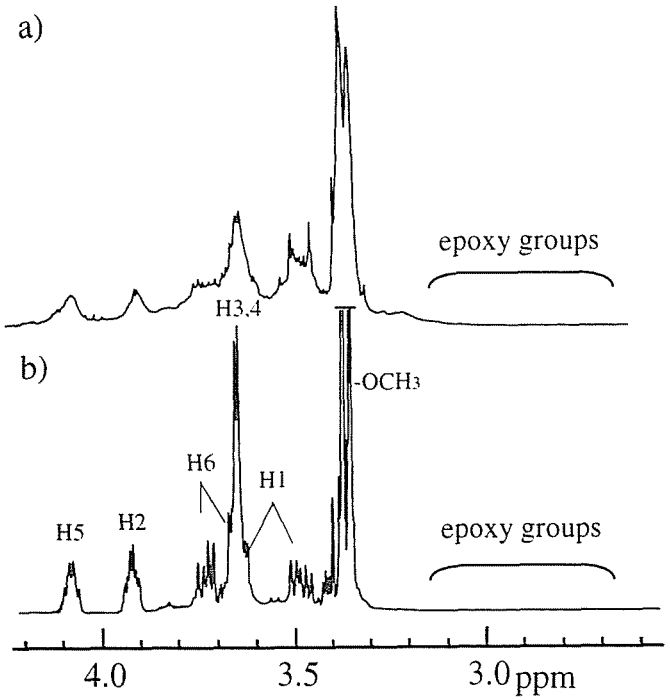
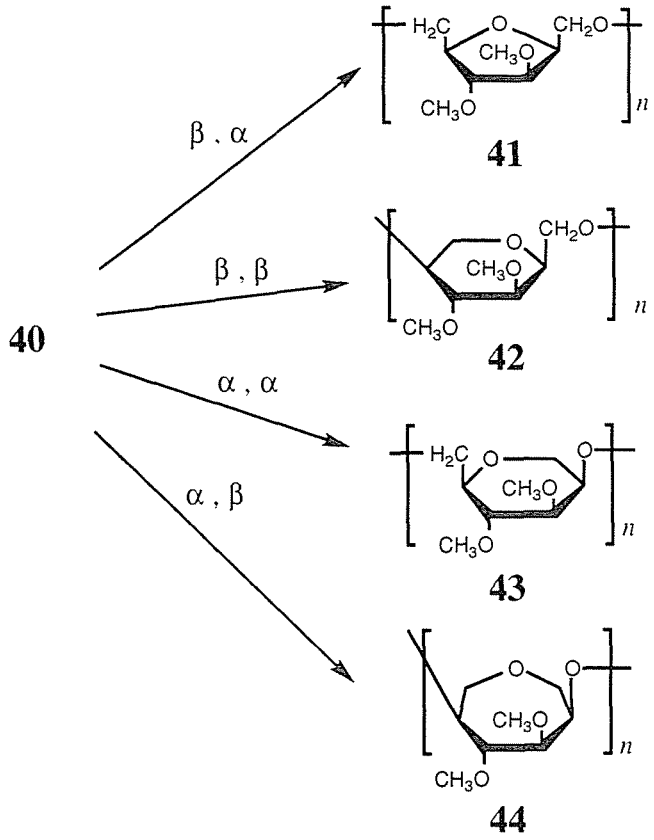


Figure 5.2. ^{1}H NMR spectra of the polymers obtained from **40** using (a) $BF_3 \cdot OEt_2$ and (b) *t*-BuOK.

opposite to that in **1**, while β,α- and α,β-scissions lead to the formation of 5- and 7-membered rings **41** and **44**, respectively, as well as **1**.

Figure 5.3 shows the ^{13}C NMR spectra of the polymers using $BF_3 \cdot OEt_2$ and *t*-BuOK. There is a distinct difference between the two spectra. In the figures, eight large and several small peaks were observed. The large peaks were assigned as follows: for the polymer using $BF_3 \cdot OEt_2$, the signals at 85.45, 84.68, 82.27 and 79.86 ppm were the methine carbons, those at 71.75 and 69.34 ppm were the methylene ones, and those at 57.34 and 57.33 ppm were the methoxy ones; for the polymer using *t*-BuOK, the signals at 85.37, 84.63, 82.23 and 79.82 ppm were the methine carbons, those at 71.68 and 69.28 ppm were the methylene ones, and those at 57.33 and 57.28 ppm were the methoxy ones. The large peaks in the polymer using $BF_3 \cdot OEt_2$ are similar to those in the polymer using *t*-BuOK. Their chemical shifts also agreed fairly well with those of the eight carbons for the polymer prepared from monomer **1** using $BF_3 \cdot OEt_2$ or *t*-BuOK. The cyclic constitutional unit in the polymers from **40**, thereby, is

Scheme 5.2 [a]



[a] The former and latter symbols correspond to the intermolecular and intramolecular scissions, respectively.

recognized as 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol, analogous to the polymer from **1**.

On the other hand, the small signals asterisked in Figure 5.3(b) are entirely attributable to both of the end units in the polymer chain, because the intensities decrease with increasing M_n of the polymer. The signals at 84.33 (CH), 84.18 (CH), 62.96 (CH_2), and 57.51 ppm (CH_3O) belonging to the small signals were very similar to those of the C4, C5, C6 and CH_3O carbons for 2,5-anhydro-1,3,4-tri-*O*-methyl-D-glucitol (**45**), respectively, thus being attributable to the terminating end of the polymer chain. In addition, the two signals at 73.07 and 27.47 ppm were assigned to the quaternary and methyl carbons of the *tert*-butoxy group, respectively, being an initiating end. These results indicate that the polymer obtained from the cyclopolymerization of **40**

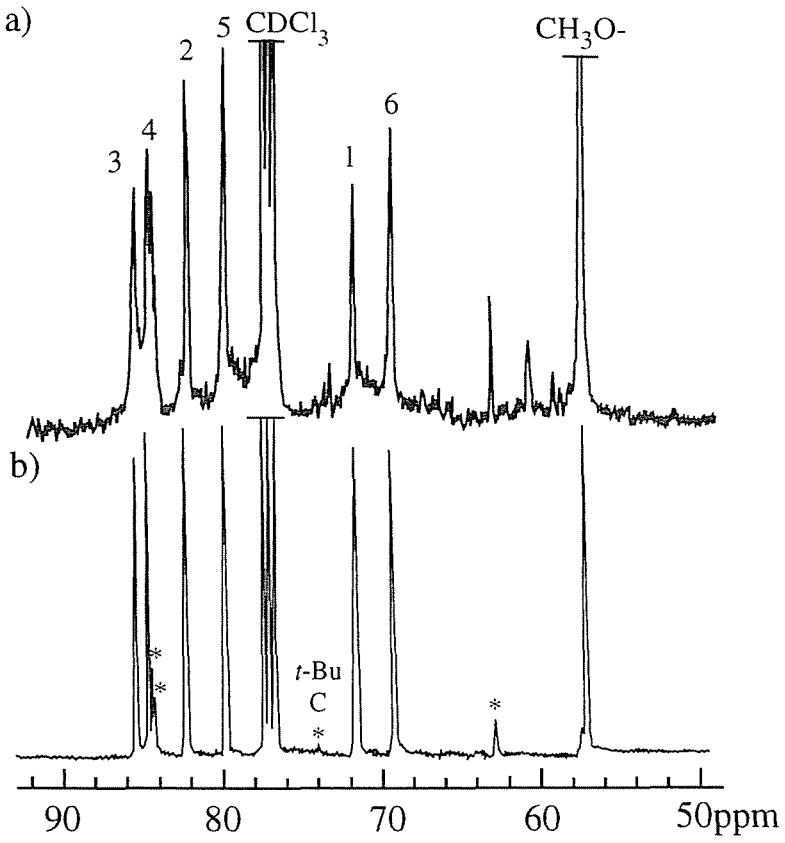
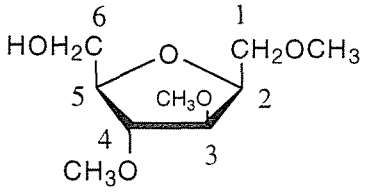


Figure 5.3. ^{13}C NMR spectra of the polymers obtained from **40** using (a) $BF_3 \cdot OEt_2$ and (b) *t*-BuOK.

using *t*-BuOK is exclusively composed of (1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol with the *tert*-butoxy and hydroxymethyl groups at both ends of the polymer chain. For the spectrum in Figure 5.3(a), a part of small signals are also due to both of the end units in the polymer chain. However, other small signals are observed. This indicates that the polymer obtained using cationic initiator should contain a slight amount of other cyclic repeating unit except for 2,5-anhydro-D-mannitol. Therefore the anionic polymerization of **40** was more stereospecific than the cationic one. These results are very similar to a relation between the cationic and anionic polymerizations of **1**.

Chart 5.1



45

C	δ/ppm
1	70.66
2	79.70
3	84.47
4	84.29
5	84.22
6	62.85
CH_3O	59.20
CH_3O	57.71
CH_3O	57.65

5.3.2 Oligomer structure

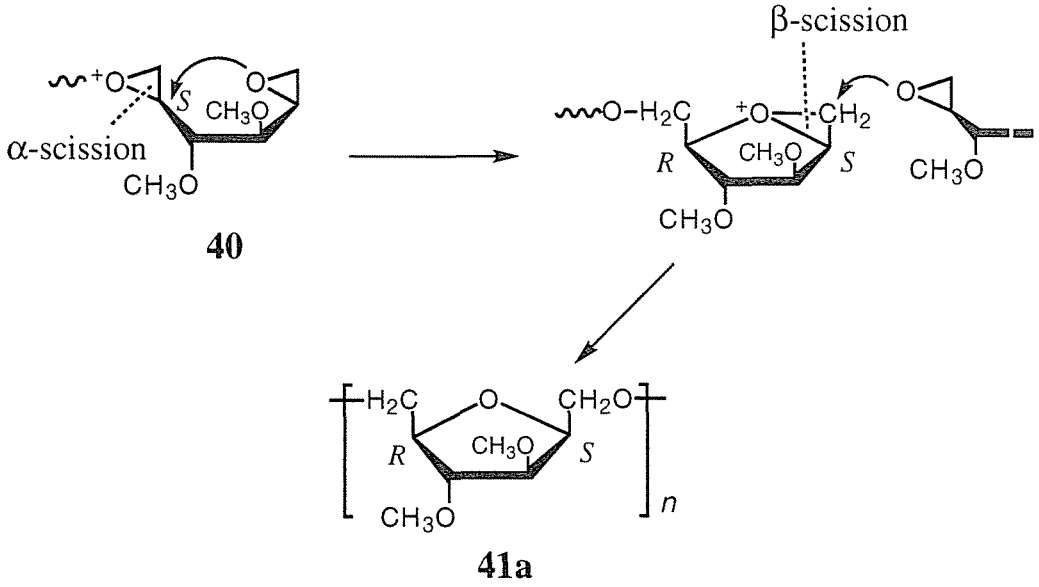
Most of the monomers were retained for the polymerization using $SnCl_4$. On the other hand, after consuming almost all of the monomers, the polymerization using BF_3•OEt_2 gave the appropriate amount of the *n*-hexane-soluble products together with the *n*-hexane-insoluble polymers. By purification using preparative thin layer chromatography, an identical compound with *m/z* = 174 and $[\alpha]^{22}_{546}$ = -22.8° (*c* 1.0, $CDCl_3$) was isolated in a 18 % yield. The structure of the isolated product was confirmed to be 1,6:2,5-dianhydro-3,4-di-*O*-methyl-D-glucitol (**19**), as in analogy with the case of **1**. In addition, the compound with *m/z* = 348 was obtained in 10 % yield for **40**, which was estimated to be 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol as the cyclic dimer (**22**). In anionic polymerization, no oligomers were formed.

5.3.3 Cyclopolymerization mechanism

The cationic polymerization of **40** produced the polymer **41a** consisting mainly of 2,5-anhydro-D-glucitol unit. Scheme 5.3 illustrates the proposed mechanism. The intramolecular cyclization proceeds through the ring opening of the first epoxide with inversion of the configuration by an S_N2 attack of the

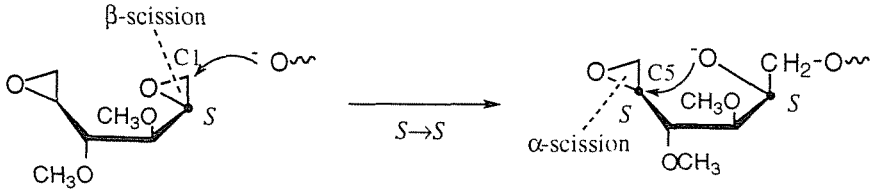
second epoxide function on the α-carbon of the former oxonium ion (α-scission); the inversion of *S*→*R*. The ring opening of the second epoxide takes place at the β-carbon with retention of the configuration on the C5 carbon, the β-carbon at which the attack is sterically favorable during the intermolecular propagation (β-scission); the retention of *S*→*S*.

Scheme 5.3

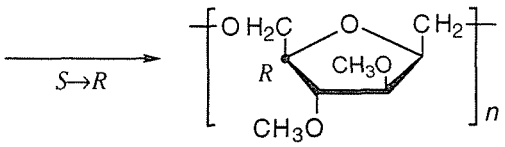


On the other hand, the anionic cyclopolymerization mechanism are indicated in Scheme 5.4. The intermolecular reaction through β-scission retains the *S* configuration of the C2 carbon. The intramolecular cyclization through α-scission inverts the configuration from *S* to *R* for the C5 carbon. The nucleophilic substitution at the α-carbon converted the L-iditol unit in monomer **40** to a D-glucitol unit in polymer **41b**. The cationic and anionic cyclopolymerizations of **40**, thus, are regio- and stereoselective, as in the case of **1**.

Scheme 5.4



40



41b

5.3.4 Direction of chain in D-mannitol and -L-iditol polymers

There is an essential difference in structure between polymers **25a** and **41b** obtained by the anionic polymerizations of **1** and **40**. Although both polymers have apparently the same constitutional repeating unit, their units differ from one another in direction. Polymer **25a** is constructed by the (1→6)-bonded unit, but polymer **41b** by the (6→1)-bonded unit, as shown in Scheme 5.5. For the intermolecular propagation of **1**, the attack by the growing alkoxide ion, which is attached at the C1 carbon, occurs at the C6-carbon of a monomer, whereas, for **40**, the alkoxide ion, which is bound to the C6 carbon, attacked the C1 carbon of a monomer. The spectral analysis of the homopolymers, however, are useless for clarifying a presence of the two bonding modes. The copolymerization between monomers **1** and **40** offers a solution to the problem of direction.

The result of the copolymerization between **1** and **40** carried out using *t*-BuOK in toluene is shown in Table 5.3. The reaction was terminated at a lower conversion to attempt an analysis of the sequences in the resulting copolymer.

Scheme 5.5

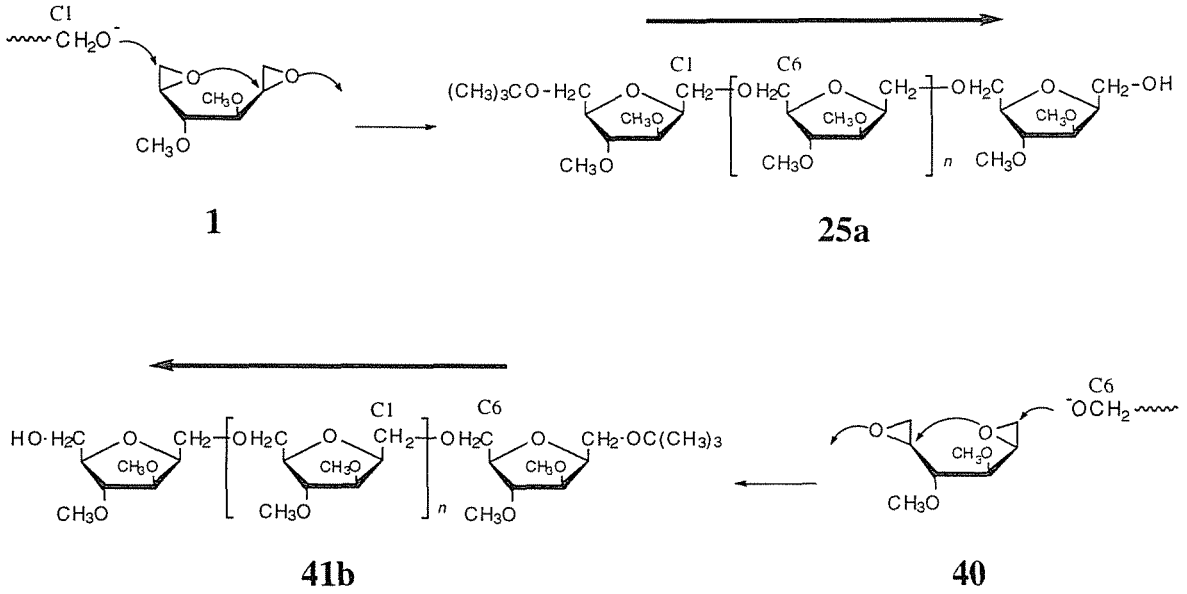


Table 5.3. Anionic copolymerization of 1,2;5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (1) (M_1) and 1,2;5,6-dianhydro-3,4-di-*O*-methyl- L-iditol (40) (M_2) using *t*-BuOK[a]

M_1/M_2 in feed	Yield (%)	M_n [b]	M_w/M_n [b]	DP_n	M_1/M_2 [c] in copolymer
0.1 / 0.9	15.6	2060	1.47	11.8	0.09 / 0.91
0.5 / 0.5	10.3	1990	1.37	11.4	0.42 / 0.58

[a] $[M_1+M_2]$=1.0 mol•L^{-1}; $[M_1+M_2]$/[Cat.]=20; temp. 60℃; time, 1h; solv., toluene. [b] Measured in THF by GPC using polystylene as the standard. [c] Determined by a molar ratio of residual monomers in the copolymerization system.

The copolymerization at a $[M_1]/[M_2]$ molar ratio of 0.5/0.5 in the feed produced the copolymer with a ratio of 0.42/0.58. Monomer **40** had a higher reactivity during the copolymerization than monomer **1**. Figure 5.4 shows the ^{13}C NMR spectra of the copolymers in the range of 80~86 ppm. Each of the singlet signals due to the C3, C4, and C5 carbons was split into two or three peaks. Variation of their relative intensities with the copolymer composition

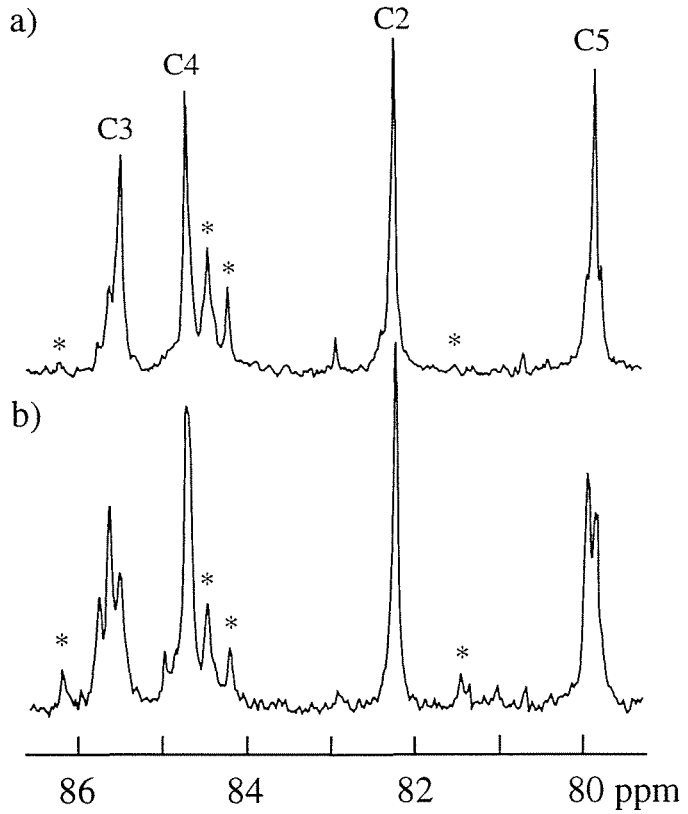
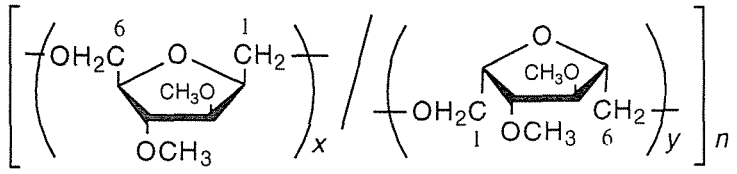


Figure 5.4. ^{13}C NMR spectra of the copolymers prepared from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) (M_1) and 1,2:5,6-dianhydro-3,4-di-*O*-methyl- L-iditol (**40**) (M_2) using *t*-BuOK in toluene: (a): M_1/M_2 of 0.09 / 0.91 in copolymer, (b): M_1/M_2 of 0.42 / 0.58 in copolymer. The asterisked signals correspond to the carbons of polymer chain-ends.

was found by comparison of Figures 5.4(a) and (b). Therefore, the copolymer is constructed by (1→6)-, (6→1)-, (1→1)-, and (6→6)-bonded 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units. The splitting is exactly caused by the difference in the sequences of the 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units. These facts elucidate the presence of two bonding modes during the homopolymerization of **1** and **40**, that is, the (1→6) and (6→1)-bonds in polymers **25a** and **41b**, respectively. The construction of the copolymer is pictured as **46** in Chart 5.2.

Chart 5.2



46

5.4 Conclusions

1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol (**40**) was cyclopolymerized by cationic and anionic catalysts to afford a gel-free polymer. The polymer prepared using cationic catalyst consisted of 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol as the main repeating units together with other cyclic units as minor components. The polymer obtained using anionic catalyst had only 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units as a result of the regio- and stereoselective mechanism, as well as the result of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**). On the other hand, the anionic copolymerization of these monomers produced a random copolymer (**46**) consisting of (1→6)-, (6→1)-, (1→1)- and (6→6)-linked 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol. For the intermolecular propagation of **1**, the attack by the growing alkoxide ion, which is attached at the C1 carbon, occurs at the C6-carbon of the monomer, whereas, for **40**, the alkoxide ion, which is bound to the C6 carbon, attacked the C1 carbon of the monomer. These results clarify the occurrence of two bonding modes during the anionic homopolymerizations of **1** and **40**, to form polymers **25a** and **41b** consisting of the (1→6) and (6→1)-bonded 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units, respectively.

5.5 Experimental Section

Measurements. ^{1}H and ^{13}C NMR spectra were recorded using a JEOL JNM-A400 II spectrometer using chloroform-d ($CDCl_3$) with tetramethylsilane as the internal standard. The molecular weights of the resulting polymers were measured by gel permeation chromatography (GPC) in tetrahydrofuran on a Jasco HPLC system equipped with three polystyrene gel columns (Shodex KF-804L). The number-average molecular weight (M_n) and the molecular weight distribution (M_w/M_n) were calculated on the basis of polystyrene calibration. Optical rotations were determined in chloroform solutions using a Jasco DIP-140 digital polarimeter.

Materials. Dichloromethane, 1,2-dichloroethane, nitrobenzene, and nitroethane were purified by the usual methods and distilled over calcium hydride. Toluene and tetrahydrofuran were purified by the usual methods and distilled from sodium benzophenone ketyl. Monomers **1** and **40** prepared according to the reported procedures were freshly distilled from calcium hydride just before use. Boron trifluoride etherate ($BF_3 \cdot OEt_2$) and tin(IV) chloride ($SnCl_4$) were purified by distillation of commercial products under reduced pressure and used as a solution in dry dichloromethane. Commercial potassium *tert*-butoxide (*t*-BuOK) was purified by sublimation before use. Potassium hydroxide (KOH) was purified by the usual methods. Column chromatography was performed on silica gel 60 (particle size 0.063-0.200 mm, Merck). Thin layer chromatography was performed on silica gel 60 F_{254} (0.25 mm thick, Merck).

1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol (40). Monomer **40** was prepared from D-mannitol.[7] Mp 38~40 °C (Lit., mp 40~42 °C); bp 65~66°C/0.3 mmHg (Lit., bp 70~72 °C/0.1 mmHg); $[\alpha]_{546}$ -9.8° (*c* 1.0 in $CHCl_3$ at 22°C); ^{1}H NMR ($CDCl_3$): δ 3.51 (s, OCH_3, 6H), 3.14~3.21 (m, epoxy CH, 2H), 3.00~3.05 (m, CH-O, 2H), 2.81 (dd, J_{gem}=5.0 Hz, $^{3}J_{cis}$=4.3 Hz, cis-CH_2, 2H), and

2.60 ppm (dd, J_{gem}= 5.0 Hz, $^{3}J_{trans}$=2.6 Hz, trans-CH_2, 2H); ^{13}C NMR ($CDCl_3$): δ 82.95 (*C*H-OCH_3), 58.64 (OCH_3), 52.03 (CH), and 42.83 ppm (CH_2).

2,5-anhydro-1,3,4-tri-*O*-methyl-D-glucitol (45). A solution of **40** (0.5 g, 2.87 mmol) in methanol containing a drop of hydrochloric acid was stirred at room temperature for 24 h. The mixture was neutralized by adding methanolic sodium methoxide and then evaporated under reduced pressure. The residue was purified by column chromatography to yield compound **45** (0.36 g, 60 %). $[\alpha]_D$ +80.5°, $[\alpha]_{577}$ +85.4°, $[\alpha]_{546}$ +94.4°, $[\alpha]_{435}$ +156.7°, and $[\alpha]_{405}$ +187.7° (*c* 1.0 in $CHCl_3$ at 23°C); ^{1}H NMR ($CDCl_3$): δ 4.13 (dt, *J*=6.6 Hz, *J*=4.3 Hz, H2, 1H), 3.93 (td, *J*=3.4 Hz, *J*=3.1 Hz, H5, 1H), 3.85 (br d, *J*=11.7 Hz, H6, 1H), 3.80 (dd, *J*=3.5 Hz, *J*=1.3 Hz, H4, 1H), 3.70 (dd, *J*=3.9 Hz, *J*=1.2 Hz, H4, 1H), 3.69~3.56 (m, H6 and H1, 3H), 3.41 (s, -OCH_3, 6H), 3.39 (s, -OCH_3, 3H), and 2.37 ppm (br s, OH, 1H); ^{13}C NMR ($CDCl_3$): δ 84.47 (C3), 84.29 (C4), 84.22 (C5), 79.70 (C2), 70.66 (C1), 62.85 (C6), 59.20 (-OCH_3 on C1), 57.71 and 57.65 ppm (-OCH_3 on C4 and C3); Anal. Calcd for $C_9H_{18}O_5$: C, 52.41; H, 8.80. Found: C, 51.61; H, 8.74; FI-MS: *m/z* (relative intensity): 206 (M^+-89.6), 207 (MH^+-100), 208 (13.8), 413 ($(2M+H)^+$-44.1), and 414 (11.6).

Cationic polymerization. Monomer **40** (500 mg, 2.87 mmol) was dissolved in dry CH_2Cl_2 (5.74 mL), and then BF_3•OEt_2 (3.62 μL, 0.0287 mmol) was added using a microsyringe. After 24 h at 0 °C, the solution was poured into a large amount of methanol containing a drop of aqueous ammonia, and the solvent was then evaporated under reduced pressure. The residue was washed using *n*-hexane and dried under vacuum to give 227 mg (45.4 % yield) of the polymer; the M_n and M_w/M_n were 1,430 and 1.97, respectively. $[\alpha]_D$ +35.2°, $[\alpha]_{577}$ +36.7°, $[\alpha]_{546}$ +43.1°, $[\alpha]_{435}$ +70.4°, and $[\alpha]_{405}$ +82.6° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR ($CDCl_3$): δ 85.45 (CH), 84.68 (CH), 82.27 (CH), 79.86 (CH), 71.74 (CH_2), 69.34 (CH_2), and 57.34 ppm (OCH_3).

The *n*-hexane-soluble products for **40** were isolated by the following procedure. Evaporation of the fractions having an R_f 0.48 (ethyl acetate/*n*-

hexane = 1/1) gave 90 mg (18 % yield) of compound **19**. Evaporation of the fractions having R_f 0.25 gave 50 mg (10.0 % yield) of compound **22**.

Anionic Polymerization. The anionic polymerizations of **40** using *t*-BuOK and KOH were carried out by the procedure described in Chart 3.The polymer was prepared using the [**40**]/[*t*-BuOK] molar ratio of 20 in toluene at 85 h (98.6 % yield). The M_n and M_w/M_n were 3390 and 1.54, respectively. $[\alpha]_D$ +77.5°, $[\alpha]_{577}$ +80.7°, $[\alpha]_{546}$ +91.5°, and $[\alpha]_{435}$ +149.6° (*c* 1.0 in $CHCl_3$ at 23 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.11~4.15 (m), 4.09 (td, *J*=5.5 Hz, *J*= 3.9 Hz, H5), 3.93 (td, *J*= 6.0 Hz, *J*= 3.0 Hz, H2), 3.74 (dd, *J*= 10.3 Hz and *J*= 5.2 Hz, H6), 3.70~3.86 (m), 3.61~3.69 (m, H3, H4, H1, and H6), 3.45~3.51 (m, H1), 3.40~3.43 (m), 3.38 (s, CH_3O), 3.36 (s, CH_3O) and 1.19 ppm (s, CH_3, *t*-BuO); ^{13}C NMR (100 MHz, $CDCl_3$): δ 85.37 (C3), 84.63 (C4), 84.33 (CH), 84.18 (CH), 82.23 (C2), 79.82 (C5), 73.07 (C, *t*-BuO), 71.68 (C1), 69.28 (C6), 62.96 (CH_2), 57.51 (CH_3), 57.33 (CH_3O), 57.28 (CH_3O), and 27.47 ppm (CH_3, *t*-BuO).

Anionic copolymerization. The copolymerization of **1** (M_1) and **40** (M_2) were carried out using *tert*-BuOK in toluene at 1 h. The copolymer was obtained using a $[M_1]/[M_2]$ molar ratio of 0.5/0.5 in the feed (10.3 % yield). The M_n and M_w/M_n were 1990 and 1.37, respectively. The M_1/M_2 molar ratio in copolymer was 0.42/0.58, which was evaluated using ^{1}H NMR measurement from the molar ratio of residual monomers in the copolymerization system. $[\alpha]_D$ +67.7° and $[\alpha]_{546}$ +87.3° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR (100 MHz, $CDCl_3$): δ 86.13 (CH), 85.69 (CH), 85.56 (CH), 85.44 (CH), 84.92 (CH), 84.78 (CH), 84.64 (CH), 84.40 (CH), 84.14 (CH), 82.21 (CH), 81.44 (CH), 81.36 (CH), 79.92 (CH), 79.84 (CH), 73.02 (C, *tert*-BuO), 71.87 (CH_2), 71.71 (CH_2), 69.35 (CH_2), 69.27 (CH_2), 62.93 (CH_2), 61.43 (CH_2), 57.67 (CH_3), 57.59 (CH_3), 57.37 (CH_3), 57.24 (CH_3), and 27.44 ppm (CH_3, *t*-BuO).

5.6 References

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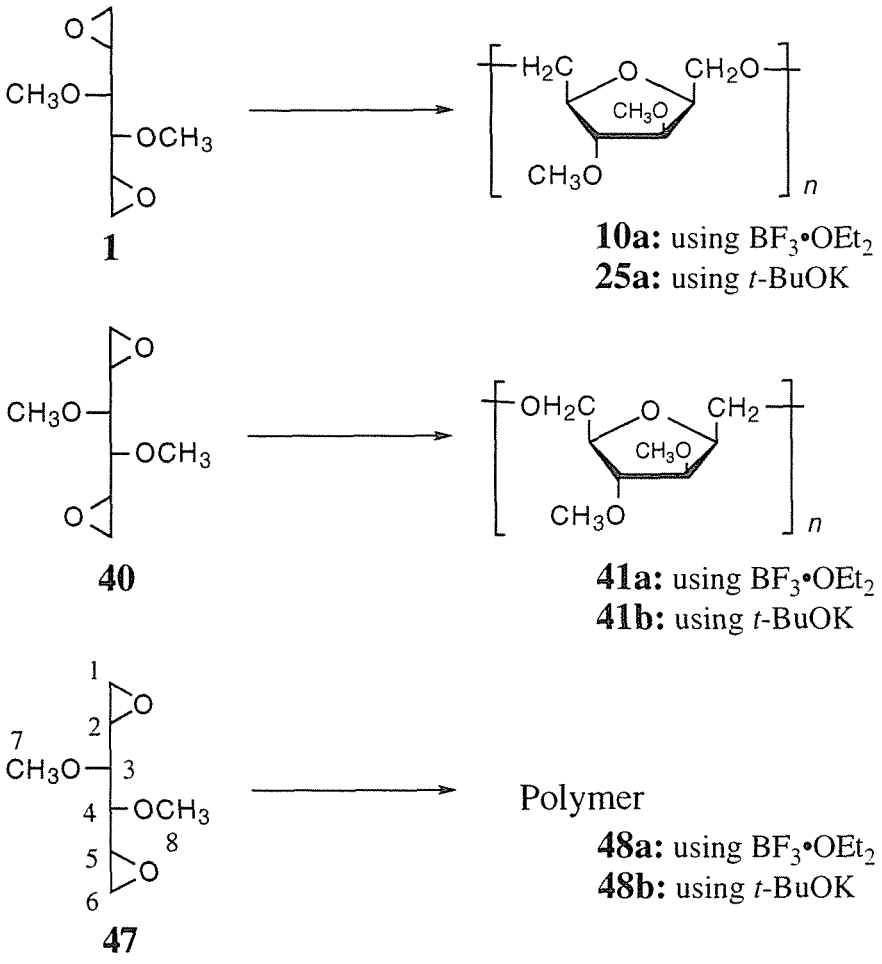
(7) Kuszmann, J. *Carbohydr. Res.* **1979**, 71, 123.

Cyclopolymerization of 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-D-glucitol to Form the Polymer Consisting of 2,5-Anhydro-3,4-di-*O*-methyl-D-mannitol and/or -L-iditol Units

6.1 Introduction

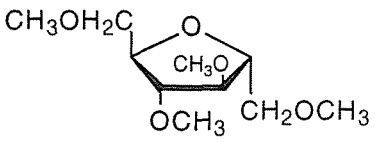
Both 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) and -L-iditol (**40**) were cyclopolymerized using boron trifluoride etherate (BF_3•OEt_2) to produce a polymer consisting mainly of 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol as the constitutional cyclic unit.[1-3] The anionic cyclopolymerizations of **1** and **40** using potassium *tert*-butoxide (*t*-BuOK) was highly regio- and stereoselective and the polymer obtained had a stereospecific structure, i.e., (1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol.[4-6] D-Mannitol and L-iditol have a center of C_2 symmetry, and the two epoxy groups in the monomer are equal in reactivity. This symmetric character is responsible for producing a polymer consisting of a single constitutional unit. Therefore, it is interesting to elucidate the character of 1,2:5,6-dianhydrohexitol with C_1 symmetry in cyclopolymerization. There are ten hexitols which contain two meso forms and four pairs of optical enantiomers. Two pairs of D- and L-isomers in mannitol and iditol are C_2 symmetric and the other pairs are asymmetric. D-Glucitol is contained in the latter pairs and, therefore, 1,2:5,6-dianhydro-D-glucitol possesses two epoxy groups whose reactivities are nonequivalent.

Scheme 6.1

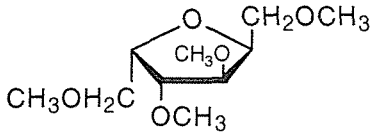


This chapter describes the cyclopolymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-glucitol (**47**) using cationic and anionic catalysts. The structures of the polymers are discussed by comparing their ^{13}C NMR spectra with those of 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-mannitol (**26**), -L-iditol (**27**) and -D-glucitol (**14**) as model compounds. The polymer prepared using BF_3•OEt_2 was composed mainly of 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol as the constitutional cyclic unit corresponding to **26**. On the other hand, the polymer prepared using *t*-BuOK contained two kind of cyclic units corresponding to **26** and **27** (Scheme 6.1).

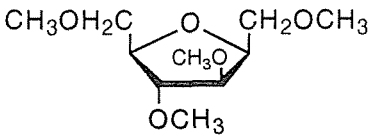
Chart 6.1



26



27



14

6.2 Results

6.2.1 Characteristics of monomer

1,2:5,6-Dianhydro-3,4-di-*O*-methyl-D-glucitol (**47**) was prepared from D-glucitol according to the reported procedure.[1] At room temperature, monomer **47** is colorless syrup. The ^{13}C NMR spectrum of the monomer has eight peaks (Figure 6.1), although those of monomers **1** and **40** have only four peaks. The ^{13}C NMR spectrum was similar to that composed to the signals of **1** and **40**. The results obtained from NMR measurements mean that **47** has two different kinds of the epoxy groups in which one of their configurations is similar to that for **1** and the other for **40**.

6.2.2 Polymerization

The cationic polymerizations of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-glucitol (**47**) using $BF_3 \cdot OEt_2$ and $SnCl_4$ proceeded homogeneously up to high conversion under the conditions, given in Table 6.1. The obtained polymers were yellowish-brown semisolids, and soluble in chloroform, methanol, tetrahydrofuran, and water, but insoluble in *n*-hexane. The polymerization

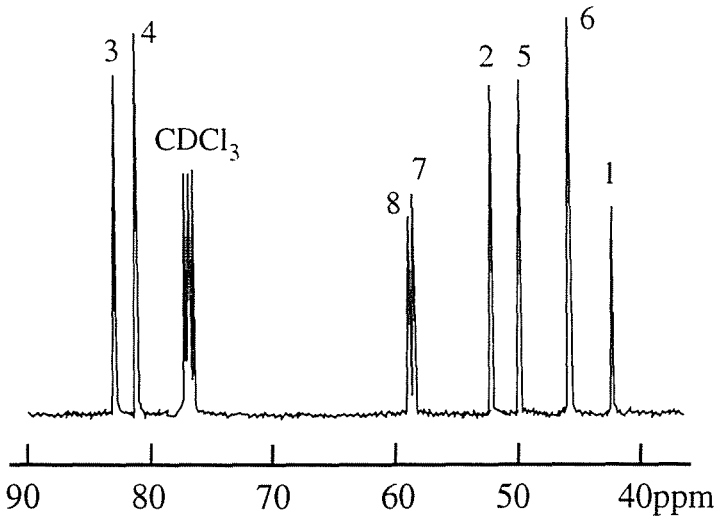


Figure 6.1. ^{13}C NMR spectrum of 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-D-glucitol (**47**).

using $BF_3 \cdot OEt_2$ in toluene exceptionally gave the organic solvent-insoluble polymer in a 14.5 % yield together with the soluble polymer in a 7.4 % yield. The yields and number-average molecular weights (M_ns) for the polymers obtained in dichloromethane and nitroethane using $BF_3 \cdot OEt_2$ were higher than those for the others. For the polymer in the system of $BF_3 \cdot OEt_2$ / CH_2Cl_2, the yield and M_n were 71 % and 3770 corresponding to the number-average degree of polymerization (DP_n) of 22, respectively.

Table 6.2 lists the results of the polymerization of **47** using *t*-BuOK. The polymerization systems were homogeneous and gradually colored brown. The resulting polymers were viscous liquids and soluble in organic solvents and water as in the case of those obtained using cationic initiators. M_ns were 4530 to 5510 with an M_w/M_n value of 1.48~1.71. Specific rotations ($[\alpha]^{22}_{546}$) were +40.6° to +62.7° for the polymers using $BF_3 \cdot OEt_2$ and $SnCl_4$, and +69.2° to +81.4° for those using *t*-BuOK (*c* 1.0 in $CHCl_3$). For both polymers, the specific rotation should be affected by the composition of constitutional units and the M_n.

Table 6.1. Cationic polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-glucitol (47) [a]

Catalyst	Solvent	Yield %	M_n [b]	M_w/M_n [b]	DP_n	$[\alpha]^{22}_{546}$ [c]
$BF_3 \cdot OEt_2$	CH_2Cl_2	70.9	3770	3.77	21.7	+50.2°
	$C_6H_5CH_3$	7.4 [d]	2010	5.05	11.6	+52.6°
	$C_2H_5NO_2$	81.8	3340	3.68	19.2	+62.7°
$SnCl_4$	CH_2Cl_2	8.1	1370	1.55	7.9	+40.6°
	$C_6H_5CH_3$	5.2	1430	1.61	8.2	+55.0°
	$C_2H_5NO_2$	12.4	1090	1.43	6.3	+61.9°

[a] [**47**]=0.5 mol•L^{-1}; [**47**]/[Cat.]=100; temp., 0 ℃; time, 24 h. [b] Measured in THF by GPC using poly(styrene) as standard. [c] Measured in $CHCl_3$ (*c* 1.0). [d] Yield of the organic solvent-insoluble polymer was 14.5%.

Table 6.2. Polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-glucitol (47) with *t*-BuOK [a]

Solvent	Yield %	M_n [b]	M_w/M_n [b]	DP_n	$[\alpha]^{22}_{546}$ [c]	y / x [d]
1,4-Dioxane	79.4	5510	1.59	31.7	+69.2°	1.5
THF	79.5	4960	1.71	28.5	+81.4°	1.5
$C_6H_5CH_3$	88.0	4530	1.48	26.0	+76.7°	1.3

[a] [**47**]=1.0 mol•L^{-1}; [**47**]/[*t*-BuOK]=20; temp., 60 ℃; time, 48 h. [b] Measured in THF by GPC using poly(styrene) as standard. [c] Measured in $CHCl_3$ (*c* 1.0). [d] Values determined by ^{13}C NMR using inverse gated spin decoupling. The area ratios of C1, C2, and C3 in 2,5-anhydro-3,4-di-*O*-methyl-L-iditol unit to those in -D-mannitol unit were estimated, respectively, and the values were avaraged.

6.2.3 Polymer structure

Figure 6.2 shows the ^1H NMR spectra of the polymers obtained using $BF_3 \cdot OEt_2$ and *t*-BuOK. The characteristic signals in the range of 2.5 to 3.2 ppm due to the epoxy groups completely disappeared and, therefore, the extent of cyclization was 100 %, i.e., both polymerizations proceeded according to a

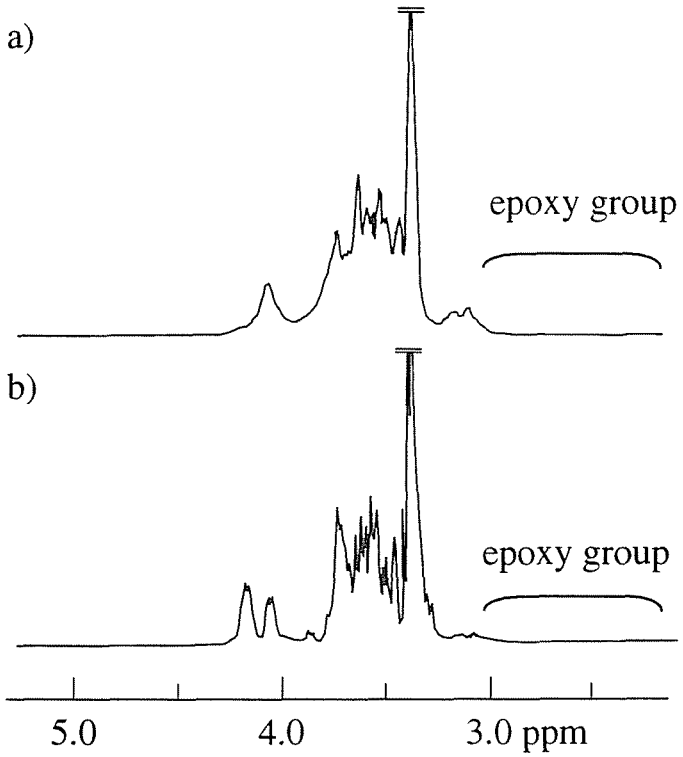


Figure 6.2. ^{1}H NMR spectra of polymers prepared from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-glucitol (**47**) using (a) $BF_3 \cdot OEt_2$ in dichloromethane and (b) *t*-BuOK in toluene.

cyclopolymerization mechanism leading to the polymers with cyclic constitutional repeating units. In both spectra, an apparent difference was observed in the regions of 3.4~4.4 ppm, which suggests the difference in stereochemistry between the polymers from the systems of $BF_3 \cdot OEt_2$ and *t*-BuOK.

For the cyclopolymerizations of **1** and **40**, the cyclic constitutional unit in the polymers was a five-membered ring, as shown in Scheme 6.1. In order to confirm the cyclic structural unit in polymer obtained from **47**, the ^{13}C NMR spectra of the polymers were compared with those of three 2,5-anhydrohexitols, i.e., 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-mannitol (**26**), -L-iditol (**27**), and -D-glucitol (**14**). Table 6.3 summarizes the ^{13}C NMR chemical shifts of these compounds. Although ten peaks were present in the spectrum of **14**, only five peaks were found in each of the spectra of **26** and **27**, which reflects the C_2 symmetry of the compounds.

Table 6.3. ^{13}C NMR chemical shifts of 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-mannitol (26), -L-iditol (27), and -D-glucitol (14) [a]

	C1	C2	C3	C4	C5	C6	3,4-*O*-CH_3	1,6-*O*-CH_3
					δ/ppm			
26	72.78	81.30	86.70	86.70	81.30	72.78	57.52	59.21
27	70.71	78.53	83.29	83.29	78.53	70.71	58.03	59.14
14	73.15	82.26	85.69	84.75	79.83	70.66	57.35, 57.42	59.19, 59.25

[a] All values were measured in $CDCl_3$ solution using tetramethylsilane as a reference.

The ^{13}C NMR spectra also were apparently different between the polymers in the systems of BF_3•OEt_2 and *t*-BuOK, as shown in Figure 6.3. For the polymer using BF_3•OEt_2, four main peaks at 86.77, 81.51, 71.59 and 57.56 ppm were assigned to the methine, methine, methylene and methoxy carbons, respectively, and thus the polymer resembles **26** very closely in chemical shifts. The structure of the polymer using cationic catalysts thereby should be mainly 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol as the five-membered constitutional unit. Several weak absorptions found in the spectrum of the polymer (Figure 6.3a), however, indicate that there might exist six- and seven-membered rings as minor constitutional units together with the 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol as major unit.

The spectrum of the polymer using *t*-BuOK consists of eight main peaks in which four peaks at 86.72 (methine), 81.43 (methine), 71.58 (methylene), and 57.52 ppm (methoxy) are similar to those assigned to the carbons of C3,4, C2,5, C1,6, and the methoxy groups for **26**, respectively, and the other four peaks at 83.21 (methine), 78.71 (methine), 69.35 (methylene), and 58.10 ppm (methyl) are close to those for **27** in chemical shifts. Therefore, the polymer obtained by anionic polymerization consists of two cyclic repeating units, 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol and -L-iditol, as seen in Scheme 6.2. The peaks observed in Figure 6.3b were slightly broad and some of them split into two bands. This should be caused by the differences of sequences in two kind of

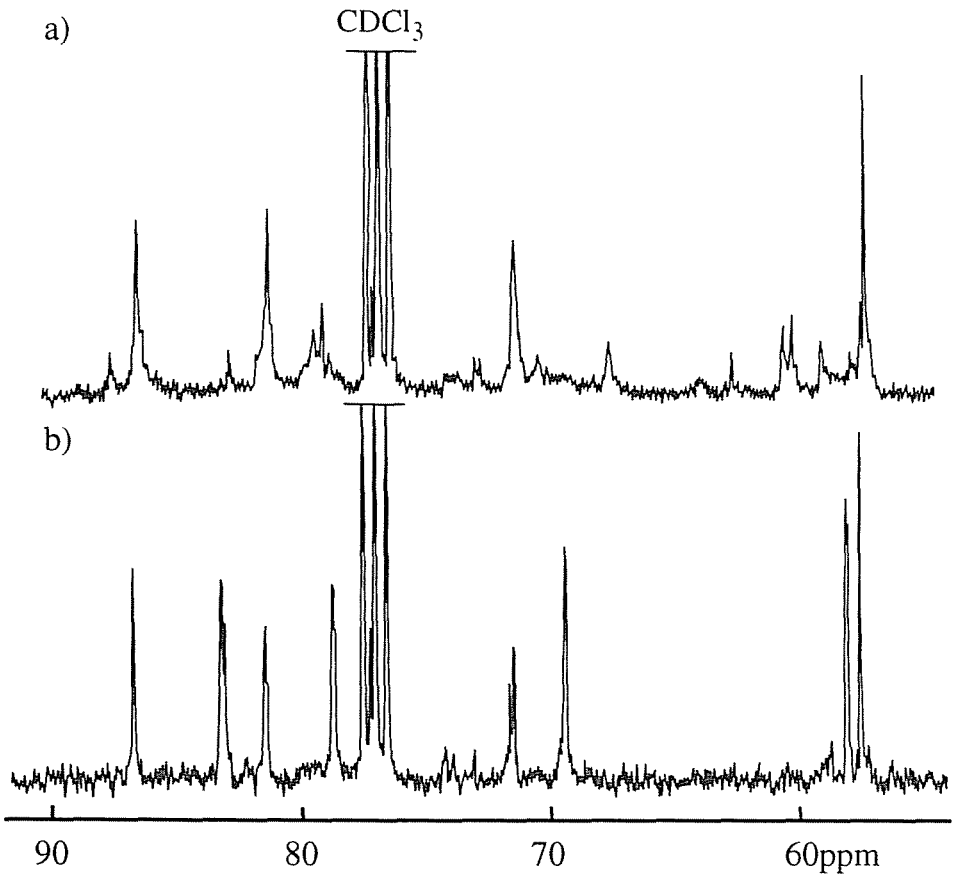
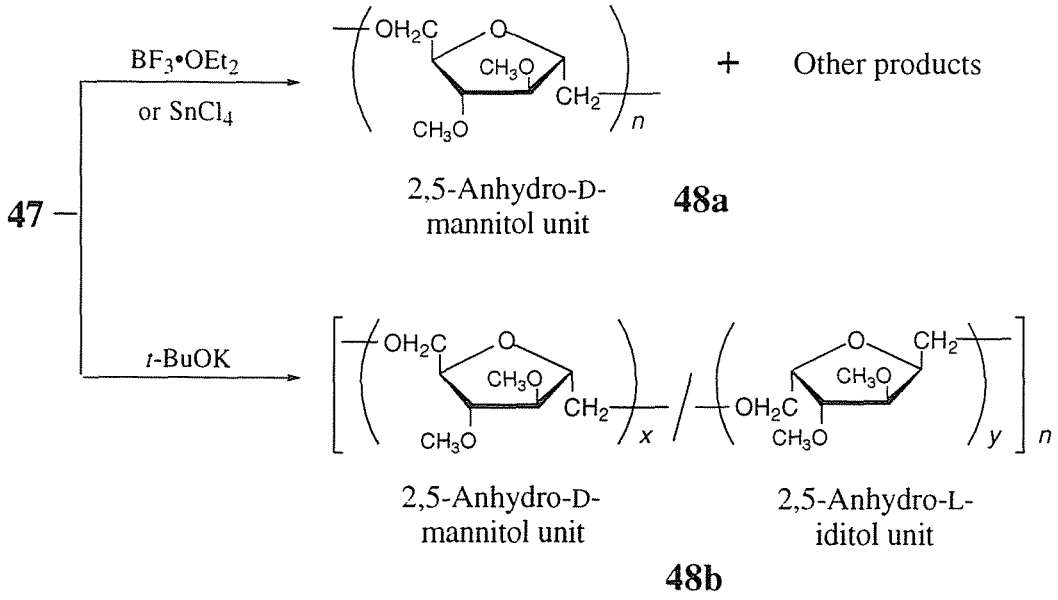


Figure 6.3. ^{13}C NMR spectra of the polymers prepared from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-glucitol (**47**) using (a) $BF_3 \cdot OEt_2$ in dichloromethane and (b) *t*-BuOK in toluene.

five-membered repeating units, because the crosspeaks corresponding to six- or seven-membered ring units could not be observed in the ^{13}C-^{1}H COSY measurement. The ratio of 2,5-anhydro-3,4-di-*O*-methyl-L-iditol units to -D-mannitol units (*y* / *x*) in the polymer was estimated by ^{13}C NMR using the inverse gated spin decoupling technique and was indicated in Table 6.2. For the anionic cyclopolymerization in 1,4-dioxane, the ratio *y* / *x* was 1.5, which means that the polymerization was favorable for forming 2,5-anhydro-3,4-di-*O*-methyl-L-iditol unit.

Scheme 6.2



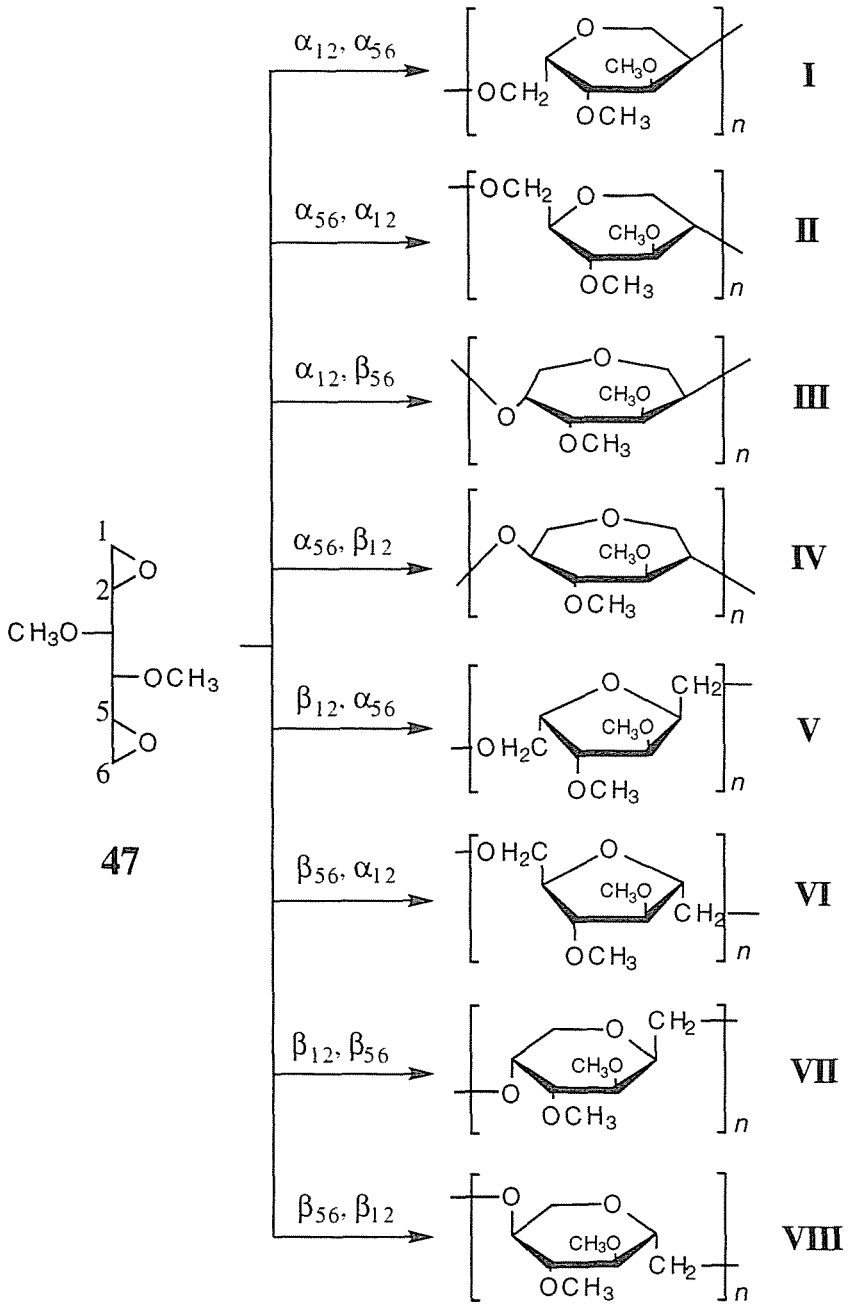
6.3 Discussion

For both polymers prepared by the cationic and anionic polymerizations of **47**, absorptions due to 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol (**14**) were not observed in the ^{13}C NMR spectra. Absence of **14** units was also confirmed by ^{13}C-^{1}H COSY. This indicates that these polymerizations would proceed through inversion of the configuration at the C2 or C5 of **47**, i.e., through the S_N2 reaction.

In monomer **47**, two epoxides at the 1,2- and 5,6-positions are different in reactivity, because of their different stereochemistry. Therefore, the possible cyclic units in the resulting polymer may be considered eight stereoisomers (**I~VIII**) formed through the S_N2-type mechanism, as shown in Scheme 6.3, where α_{12} and β_{12}, and α_{56} and β_{56} represent α- and β-scissions in the 1,2- and 5,6-epoxides, respectively. In the cyclopolymerization of **47**, the intermolecular reaction and intramolecular cyclization through α_{12},α_{56}-, α_{56},α_{12}-, β_{12},β_{56}-, and β_{56},β_{12}-scissions of the two epoxides in the molecule form

the 6-membered rings **I**, **II**, **VII** and **VIII**, respectively; whereas, β_{12},α_{56}- and β_{56},α_{12}-scissions lead to the formation of the 5-membered rings **V** and **VI**, and α_{12},β_{56}- and α_{56},β_{12}- scissions to that of the 7-membered rings **III** and **IV**.

Scheme 6.3 [a]

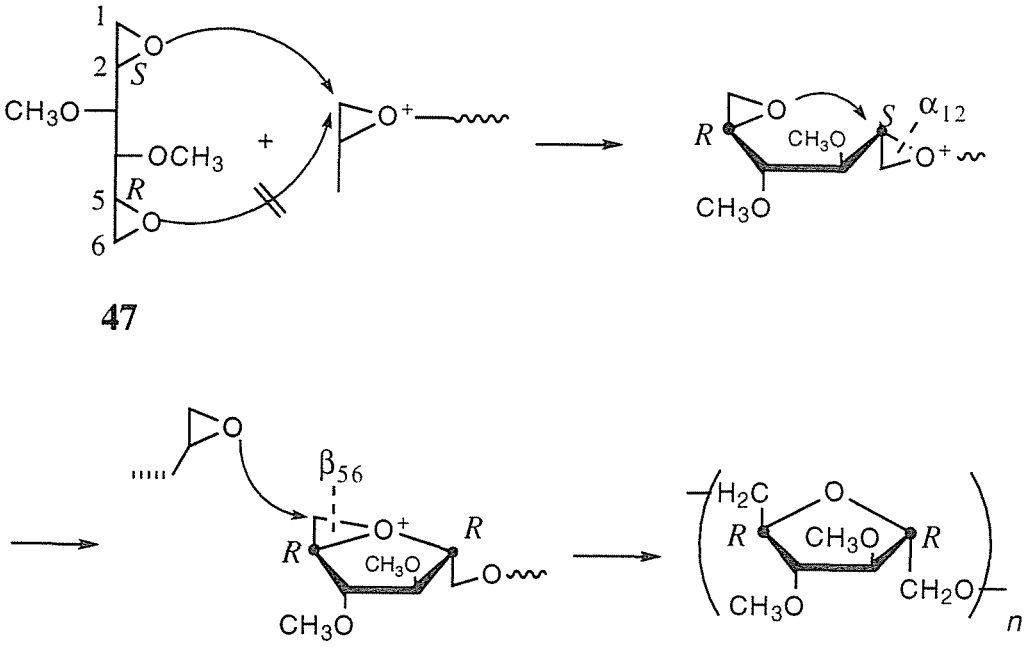


[a] Former and latter symbols correspond to intermolecular and intramolecular scissions, respectively.

Because the ^{13}C NMR spectrum of the polymer obtained using $BF_3 \cdot OEt_2$ showed that the cyclic repeating unit consists mainly of 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol **VI**, the cationic polymerization of **47** is concluded to involve β_{56},α_{12}-scissions selectively. In intramolecular cyclization, the α-carbon of the 1,2-epoxide moiety forming oxonium ion is attacked by the oxygen atom of the 5,6-epoxide, and the resulting bicyclic oxonium ion is subsequently attacked at the β-carbon by a monomer in the intermolecular reaction as shown in Scheme 6.4. The α-scission of the 1,2-epoxide moiety leads to inversion of the configuration (*S*→*R*), whereas the β-scission of the 5,6-epoxide moiety causes retention of the configuration (*R*→*R*). Thus, the formation of 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol unit **VI** results from the regio- and stereoselective mechanism. It is worth noting that the ring-opening mode of the epoxide is different for the inter- and intramolecular reactions. The former reaction takes place preferentially at the 1,2-epoxide moiety as a nucleophile between the two epoxide moieties in the monomer. Since the oxygen atom at the 5,6-epoxide in monomer **47** was interfered by methoxy groups, the reactivity of the 5,6-epoxide should be sterically more unfavorable than that of the 1,2-epoxide.

The anionic cyclopolymerization of **47** produced a polymer consisting of two cyclic repeating units, 2,5-anhydro-3,4-di-*O*-methyl-L-iditol **V** and D-mannitol **VI**. In the polymerization, the intermolecular reaction through β-scission is established with retention of configuration, but the intramolecular cyclization through α-scission occurred with inversion. In β_{12},α_{56}-scission, retention at C2 (*S*→*S*) and inversion at C5 (*R*→*S*) form cyclic unit **V** with *S*,*S*-configuration, and in the β_{56},α_{12}-scission, on the contrary, retention at the C5 (*R*→*R*) and inversion at the C2 (*S*→*R*) form cyclic unit **VI** with *R*,*R*-configuration, as shown in Scheme 6.5. The two processes competitively take place to produce a polymer consisting of 2,5-anhydro-3,4-di-*O*-methyl-L-iditol **V** and -D-mannitol **VI** with a ratio (y / x) of about 1.5. Although involving two

Scheme 6.4

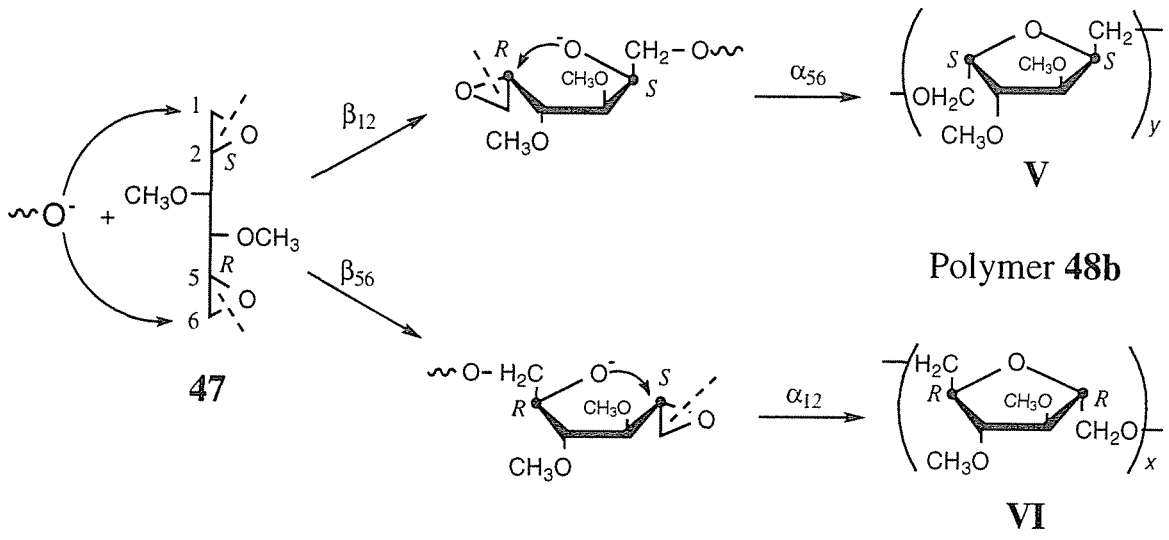


47

48a (**VI** unit)

processes, the polymerization proceeds through a regio- and stereoselective mechanism in each process. The intermolecular reaction takes place favorably at the 1,2-epoxide moiety rather than the 5,6-epoxide moiety of monomer in the anionic polymerization.

Scheme 6.5



47

V

Polymer **48b**

VI

The alternating process of β- and α-scission in the inter- and intramolecular reactions is the most striking aspect in the anionic polymerization. The superiority of α-scission in the intramolecular cyclization to form the five-membered rings in both polymerizations can be explained by the Baldwin's rule which is generally suited to ring closure on the basis of stereoelectronic effect, as described in Chapters 2 and 3.

The intramolecular cyclization of **47** was regio- and stereoselective to form five-membered repeating units, though small fraction of other cyclized units was present for the cationic polymerization and two 2,5-anhydrohexitol units were formed for the anionic polymerization.[7] For intermolecular propagation, the 1,2-epoxy group of **47** predominantly reacted with the growing chain-end, which should be caused by some differences in the stereochemistry of the transition state between the 1,2-epoxy and 5,6-epoxy groups.

6.4 Conclusions

The polymerizations of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-glucitol were carried out using cationic and anionic catalysts. The polymerizations proceeded through the cyclopolymerization mechanism leading to polymers with cyclic constitutional units. The cationic cyclopolymerization yielded a polymer consisting mainly of 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol units. The anionic polymerization involves two processes to yield a polymer consisting of 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol and L-iditol units. The intermolecular reaction exclusively selected the β_{56}-scission in the cationic polymerization but slightly favored the β_{12}-scission in the anionic polymerization. The intra- and intermolecular reactions introduced α- and β-scissions of the epoxides with inversion and retention of the configuration at the α-carbon of epoxide moiety, respectively. Conclusively, both polymerizations are regio- and stereoselective.

6.5 Experimental Section

Measurements. ^{1}H and ^{13}C NMR spectra were recorded with JEOL JNM-EX270 and JNM-A400 II. Optical rotations were determined with a Jasco DIP-140 digital polarimeter. The molecular weight of polymers was measured by gel permeation chromatography (GPC) in tetrahydrofuran on a Jasco HPLC system equipped with three polystyrene gel columns (Shodex KF-804L). The number-average molecular weight (M_n) and molecular weight distribution (M_w/M_n) were calculated on the basis of a polystyrene calibration. Thin layer chromatography was performed on silicagel 60 F_{254} (0.25 and 2.0 mm thick, Merck).

Materials. Dichloromethane and nitroethane were distilled over calcium hydride. Toluene, tetrahydrofuran, and 1,4-dioxane were purified by the usual method and distilled from sodium-benzophenone. Boron trifluoride etherate ($BF_3 \cdot OEt_2$) and tin(IV) chloride ($SnCl_4$) were purified by distillation of commercial products under reduced pressure and used as a solution in dry dichloromethane. Potassium *tert*-butoxide (*t*-BuOK) was purified by sublimation under vacuum before use. 2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol (**14**) was synthesized from **1**, as described in Chapter 2. 2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-D-mannitol (**26**) and 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-L-iditol (**27**) were prepared by methylation of 2,5-anhydro-D-mannitol and 2,5-anhydro-L-iditol, respectively (Chapter 3).

1,2:5,6-Dianhydro-3,4-di-*O*-methyl-D-glucitol (4). Monomer **47** was prepared from D-glucitol according to the reported procedure.[8] **47** was distilled over CaH_2 under reduced pressure before polymerization run. Bp 72~73 °C/0.3 mmHg; $[\alpha]_D$ -6.3°, $[\alpha]_{577}$ -8.3°, $[\alpha]_{546}$ -9.6°, $[\alpha]_{435}$ -15.6°, and $[\alpha]_{405}$ -18.8° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{1}H NMR (400 Hz, $CDCl_3$): δ 3.57 (s, CH_3O-, 3H), 3.45 (s, CH_3O, 3H), 3.10~3.21 (m, 3H), 3.03 (dd, J = 7.0 Hz, J = 3.3 Hz, 1H), 2.89 (dd, J = 5.3 Hz, J = 3.7 Hz, 1H), 2.78~2.81 (m, 2H), and 2.55 ppm (dd,

J = 4.8 Hz, J = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 83.71 and 82.03 (CH), 59.77 and 59.42 (CH_3O), 53.00 and 50.74 (CH, epoxy), and 46.68 and 43.27 ppm (CH_2, epoxy).

Cationic Polymerization. A typical polymerization procedure is as follows: Monomer **47** (0.5 g, 2.87 mmol) was dissolved in dry CH_2Cl_2 (5.74 mL), and BF_3•OEt_2 in CH_2Cl_2 (39.1 μL in 0.73 mol•L^{-1}, 0.0285 mmol) was added by a microsyringe at 0 °C. After 24 h, the reaction mixture was poured into a excess methanol containing a drop of aqueous ammonia, and the entire solution was evaporated under reduced pressure. The residue was washed with *n*-hexane several times and dried under vacuum to give the polymer (355 mg, 70.9 %). The number-averaged molecular weight (M_n) and molecular weight distribution (M_w/M_n) were 3770 and 3.77, respectively. $[\alpha]_D$ +43.9°, $[\alpha]_{577}$ +44.9°, $[\alpha]_{546}$ +50.2°, $[\alpha]_{435}$ +80.3°, and $[\alpha]_{405}$ +93.9° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR (100 MHz, $CDCl_3$): δ 86.77 (CH), 81.51 (CH), 71.59 (CH_2), and 57.56 ppm (CH_3).

Anionic Polymerization. A typical polymerization procedure is as follows: Polymerization was carried out in an H-shaped glass ampoule. *tert*-BuOK (12.2 mg, 0.11 mmol) and dry THF (2.0 mL) were added to one side of the ampoule, and **47** (0.355 g, 2.04 mmol) was added to the other side under a nitrogen atmosphere. After sealing under vacuum, the monomer and catalyst solution were mixed at 60 °C. After 48 h, the reaction mixture was poured into a excess methanol containing a drop of 0.1N hydrochloric acid, and the solution was evaporated under reduced pressure. The residue was treated as described for the cationic polymerization to give the polymer (0.282 g, 79.5 %). The M_n and M_w/M_n were 4960 and 1.71, respectively. $[\alpha]_{577}$ +73.4°, $[\alpha]_{546}$ +81.4°, $[\alpha]_{435}$ +133.0°, and $[\alpha]_{405}$ +156.2° (*c* 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR (68 MHz, $CDCl_3$): δ 86.72 (CH), 83.21 (CH), 81.43 (CH), 78.71 (CH), 71.42 (CH_2), 69.35 (CH_2), 58.10 (CH_3), and 57.52 ppm (CH_3).

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Conclusions

The polymerization tendency of 3,4-*O*-substituted 1,2:5,6-dianhydro-mannitols and their substituent effects in the 3,4-positions were studied on the cationic cyclopolymerization. The cationic polymerizations of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitols with $BF_3 \cdot OEt_2$ proceeded regio- and stereoselectively to produce the linear polymer consisting of 2,5-anhydro-D-glucitol as a main cyclic constitutional unit and 2,6-anhydro-L-iditol as a minor unit. After separating the polymer from the raw product, a large amount of 1,6:2,5-dianhydro-D-glucitols and a very small amount of other cyclic oligomers were isolated. On the other hand, 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol polymerized with $BF_3 \cdot OEt_2$ and $SnCl_4$ to yield the polymers with cyclic and acyclic units. The restriction on free rotation of the C-C bond at the 3,4-positions caused the monomer to lower the extent of cyclization to about 0.5.

The anionic cyclopolymerization of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol using potassium *tert*-butoxide and potassium hydroxide was higher regio- and stereoselective than that using cationic catalysts and produced a well-defined polymer, that is, (1→6)-3,4-di-*O*-alkyl-2,5-anhydro-D-glucitol, which has hydroxymethyl and *tert*-butoxy groups at each of the chain ends. For the polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol, the polymer yields and molecular weights were affected by the monomer to catalyst molar ratio and the polymerization time. The presence of a crown ether, 18-crown-6, in the cyclopolymerization allowed the M_n of the polymer to approach the value estimated from the [monomer]/[*t*-BuOK] molar ratio. The complexing

agent promoted the dissociation of *t*-BuOK to an initiating anion. On the other hand, 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol tended to form a gel in the polymerization process. The restriction of free rotation at the C3 and C4-positions of the monomer strongly led to the decrease in its tendency to undergo cyclization. The highly selective cyclopolymerization of 1,2:5,6-dianhydro-D-mannitol using the anionic catalyst is a new synthetic method for preparing an artificial polysaccharide.

The cyclopolymerizations of (2*S*,5*S*)-1,2:5,6-diepoxyhexane which corresponds to the 3,4-substituent-free compound of 1,2:5,6-dianhydro-D-mannitols were carried out using cationic and anionic initiators. For the polymer obtained using $BF_3 \cdot OEt_2$, the cyclic constitutional repeating units were the 5- and 6-membered rings together with a pendant epoxy group unit. The polymer using *t*-BuOK essentially consisted of the 5-membered cyclic repeating unit. The cationic cyclopolymerization has lower regio- and stereoselectivity than that of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol. On the other hand, the anionic cyclopolymerization proceeded through a highly regio- and stereoselective mechanism as well as that of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol. These results clarified that the high regio- and stereoselectivity in the anionic cyclopolymerization resulted not from the effect of substituents, but from the exact nature of 1,2:5,6-diepoxide.

The cationic and anionic cyclopolymerizations of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-L-iditol, which is a diastereomer of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol, were carried out to obtain further information on the regio- and stereoselective cyclopolymerizations of 1,2:5,6-dianhydrohexitols. The configurational relationship between the homopolymers obtained from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-L-iditol and 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol was also discussed on the basis of the copolymerization

between these monomers. 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol was cyclopolymerized by cationic and anionic catalysts to afford a gel-free polymer. The polymer prepared using cationic catalyst consisted of 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol as the main repeating units together with other cyclic units as minor components. The polymer obtained using anionic catalyst had only 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units as a result of the regio- and stereoselective mechanism, as well as the result of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol. On the other hand, the anionic copolymerization of these monomers produced a random copolymer consisting of (1→6)-, (6→1)-, (1→1)- and (6→6)-linked 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol. The results clarified the presence of two bonding modes during the anionic homopolymerizations of 1,2;5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol and -L-iditol. Consequently, the homopolymers consisted of the (1→6) and (6→1)-bonded 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units, respectively.

The cyclopolymerizations of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-glucitol, which possesses two chemically nonequivalent epoxy groups, were carried out using cationic and anionic catalysts. The polymerizations proceeded through the cyclopolymerization mechanism leading to polymers with cyclic constitutional units. The cationic cyclopolymerization yielded a polymer consisting mainly of 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol units. The anionic polymerization involved two processes to yield a polymer consisting of 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol and L-iditol units. The intermolecular reaction exclusively selected the β_{56}-scission in the cationic polymerization, but slightly favored the β_{12}-scission in the anionic polymerization. The intra- and intermolecular reactions introduced α- and β-scissions of the epoxides with inversion and retention of the configuration at the α-carbon of epoxide moiety, respectively, in both polymerizations which are regio- and stereoselective.