Syntheses of Macromolecular Ionophores via Cyclopolymerization of Diepoxides and Related Compounds

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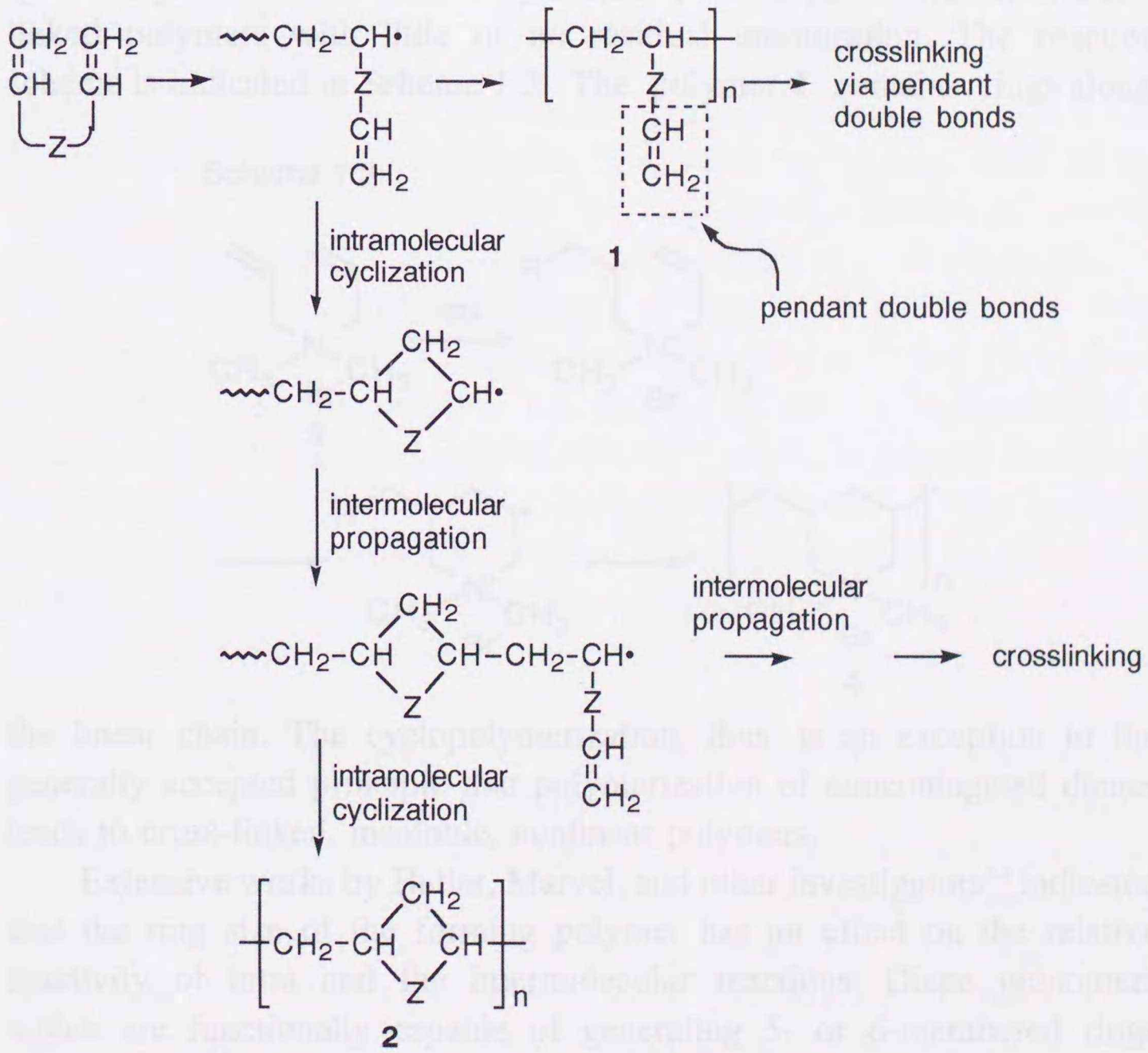
Introduction

1.1 Cyclopolymerization

Cyclopolymerization[1] is defined as a chain-growth polymerization reaction of nonconjugated dienes. The applicable monomer is subsequently extended to compounds with other types of reactive function, such as dialdehydes, diisocyanates, diepoxides, and diynes.

The nonconjugated dienes undergo a chain propagation reaction containing inter and intramolecular reaction, as depicted in Scheme 1.1,

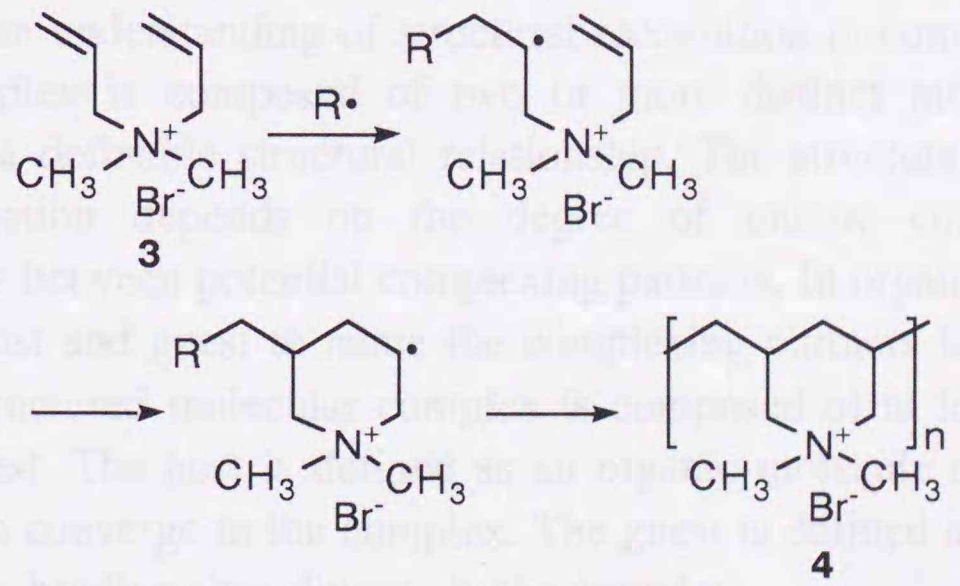
Scheme 1.1



where Z is a structural unit such as a benzene ring in divinylbenzene and a trimethylene unit in 1,6-heptadiene. The preferential occurrence of intermolecular propagation leads to produce a linear polymer **1** with pendant double bonds. An intramolecular cyclization of the propagating species with a double bond in the same recurring unit forms a cyclized active species. The alternating intra-intermolecular propagations yield a soluble, gel-free cyclopolymer **2** without residual unsaturation. A decrease in participation of the intramolecular cyclization introduces to the formation of partially cyclized soluble polymer. When the propagating species reacts with a pendant double bond in the other recurring units, cross-linked, insoluble polymers are produced. In order to form the cyclopolymer, therefore, it is important to control the relative reactivity of intra and intermolecular reactions.

Cyclopolymerization was found in the polymerization of diallyl quaternary ammonium salts **3** by Butler[2,3], which gave soluble, uncross-linked polymers with little or no residual unsaturation. The reaction scheme is indicated in Scheme 1.2. The polymer **4** contains rings along

Scheme 1.2



3 **4**

the linear chain. The cyclopolymerization, thus, is an exception to the generally accepted principle that polymerization of nonconjugated dienes leads to cross-linked, insoluble, nonlinear polymers.

Extensive works by Butler, Marvel, and other investigators[4-6] indicated that the ring size of the forming polymer has an effect on the relative reactivity of intra and the intermolecular reactions. Diene monomers which are functionally capable of generating 5- or 6-membered rings

almost invariably cyclopolymerize. 1,6-Dienes such as acrylic and methacrylic anhydride, methyl allyl maleate, and 1,6-heptadiene, and 1,6-heptadiyne yield essentially the polymers with 6-membered rings.[6-9] 1,5-Hexadiene and *o*-divinylbenzene are the examples of 1,5-dienes to give the polymers consisting of 5-membered rings.[10,11] On the other hand, the cyclopolymerization tendency falls sharply for rings of more than six atoms. Thus, the dienes forming medium and large rings need to be found the reaction conditions increasing cyclopolymerization tendency.

1.2 Crown-Type Compounds

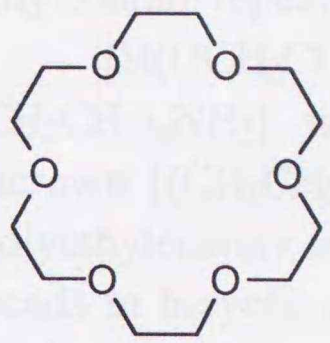
1.2.1 Crown Ethers and Related Compounds

Structural molecular complexation is central to biological phenomena. The structure of the simple compounds supplied by nature have long inspired and challenged organic chemists to develop laboratory syntheses of the same compounds. A newer challenge provided by the biotic world is the design and synthesis of abiotic systems that mimic some of the properties of biotic systems. Any response to this challenge depends directly on an understanding of structural recognition in complexation.

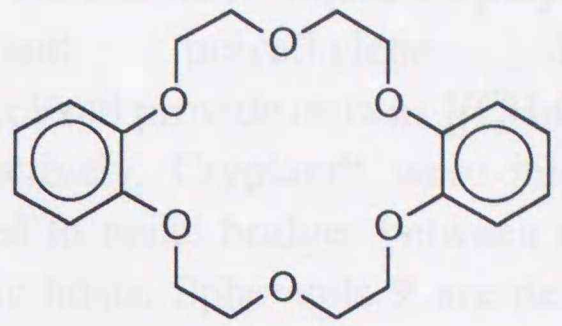
A complex is composed of two or more distinct molecules held together in a definable structural relationship. The structural recognition in complexation depends on the degree of unique complementary relationships between potential complexing partners. In organic chemistry, the terms host and guest to name the complexing partners have evolved. A highly structured molecular complex is composed of at least one host and one guest. The host is defined as an organic molecule or ion whose binding sites converge in the complex. The guest is defined as a molecule or ion whose binding sites diverge in the complex.

The design and synthesis of hosts with the specificity of enzyme and ion transport systems are particularly exciting possibilities. A remarkable progress along this line has been by three winners of 1987's Nobel prize, Pedersen[12,16], Lehn[13,16], and Cram.[14-16] In 1967, Pedersen[12] reported the synthesis of the first crown ethers which particularly bind with alkali metal ions. The crown ethers were the cyclic hexaethers **5** and **6** which have been simply called [18]crown-6 and dibenzo[18]crown-6. In 1969,

Scheme 1.3



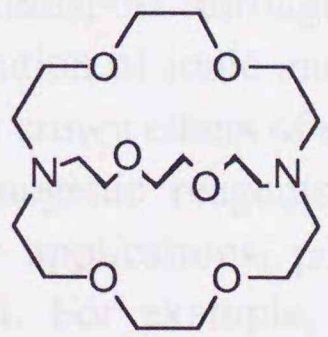
5: [18]Crown-6



6: Dibenzo[18]Crown-6

Lehn[13] devised bridging of a monocyclic crown ether with an additional oligoether chain to form so called cryptand **7**. In 1974, Cram newly synthesized chiral crown compounds **8** capable of recognizing a chiral guest and established the concept of "Host-Guest Chemistry".[15]

Scheme 1.4



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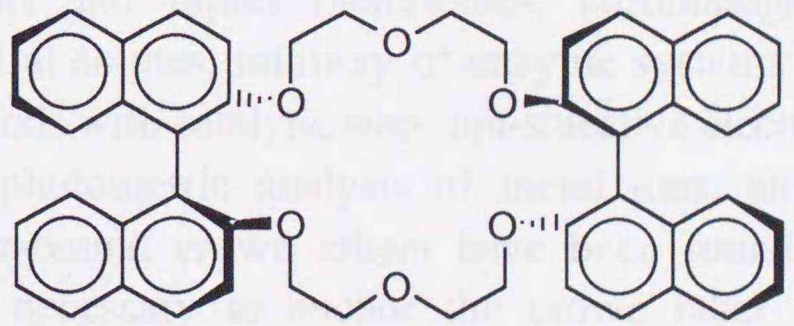

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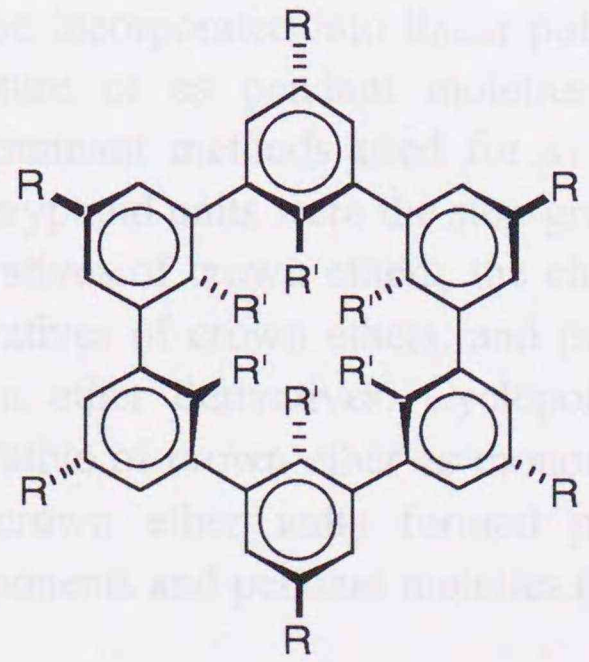

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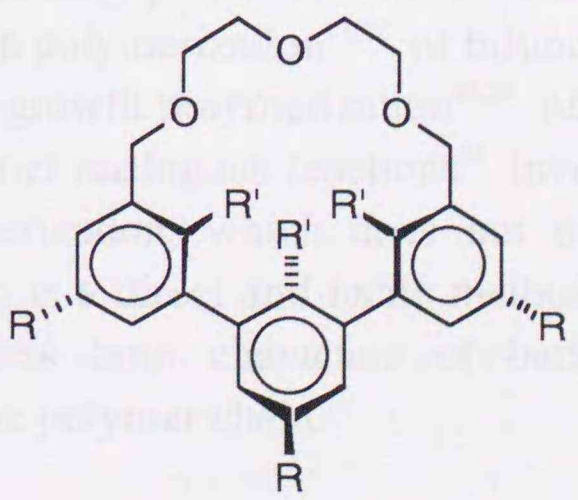

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Hosts are open-chain, cyclic, bicyclic, or polycyclic compounds that frequently contain repeating units.[17,18] The classic examples are polyethylene glycols $[H(OCH_2CH_2)_nOH]$ and polyethylene diamines $[H(NHCH_2CH_2)_nNH_2]$, which when cyclized provide crowns $[(CH_2CH_2O)_n]$ and azacrown $[(CH_2CH_2NH)_n]$, respectively. Cryptands were introduced when polyethyleneoxy units were used to make bridges between nitrogen bridgeheads in bicyclic and polycyclic hosts. Spherands **9** are defined as hosts conformationally organized prior to complexation, and composed of units much more rigid than those of crowns and cryptands. Hemispherands **10** contain contiguous rigid parts sufficient in number to dominate the general shapes of hosts.

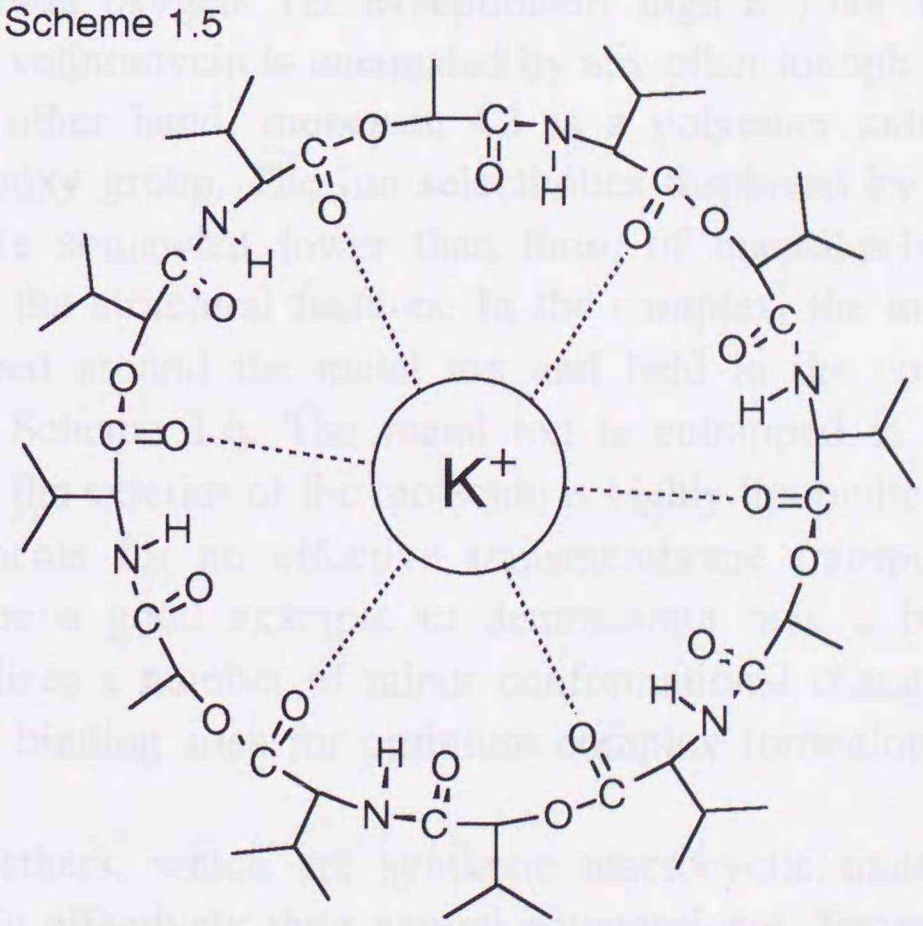
1.2.2 Crown Ethers on Polymers[19]

Crown ethers and other macroheterocyclic hosts have found application in diverse fields of science. These include phase-transfer catalysis[20], mediated ion transport through solid and liquid membranes, chromatographic separation of ionic and neutral solutes, mimicry of enzyme systems using chiral crown ethers of cryptands with catalytic sites, ion-selective electrodes, chromogenic reagents for photometric analysis of metal ions, etc. For many applications, polymer-bound crown ethers have been found very useful. For example, it is necessary to anchor the crown ether to an insoluble support like silica gel or a network polymer in phase-transfer catalysis, ion transport, and chromatographic separation. Crown ethers can be incorporated into linear polymers as components of the backbone structure or as pendant moieties anchored to a polymer chain. The predominant methods used for synthesizing polymers with crown ether and cryptand units were the step-growth polymerization[21,22] of bifunctional derivatives of crown ethers, the chain-growth polymerization[23,24] of vinyl derivatives of crown ethers, and polymer analogous reactions[25] involving crown ether derivatives. Cyclopolymerization, which does not need a derivative of crown ether as monomer, is a direct and facile method, and the crown ether units formed possess both characters of backbone components and pendant moieties in the polymer chain.

1.3 Ionophores

Ionophores[17] can be characterized as receptors which form stable, lipophilic complexes with charged hydrophilic species such as Na^+, K^+, Ca^{2+} etc. and thus are able to transport them into lipophilic phases, for example, across natural or artificial membranes. Metal ion complexes of ionophores can be considered as host-guest complexes in which the guest entity is of spherical shape and entrapped in a cavity-like structure formed by the cyclic or open-chain host molecule. Very often, the processes of complexation and transport are highly specific. Many of the ionophores display the ability of discrimination between alkali metal ions of different size. Valinomycin **11** has a 10^4 times greater affinity to potassium than to sodium ions.

Scheme 1.5



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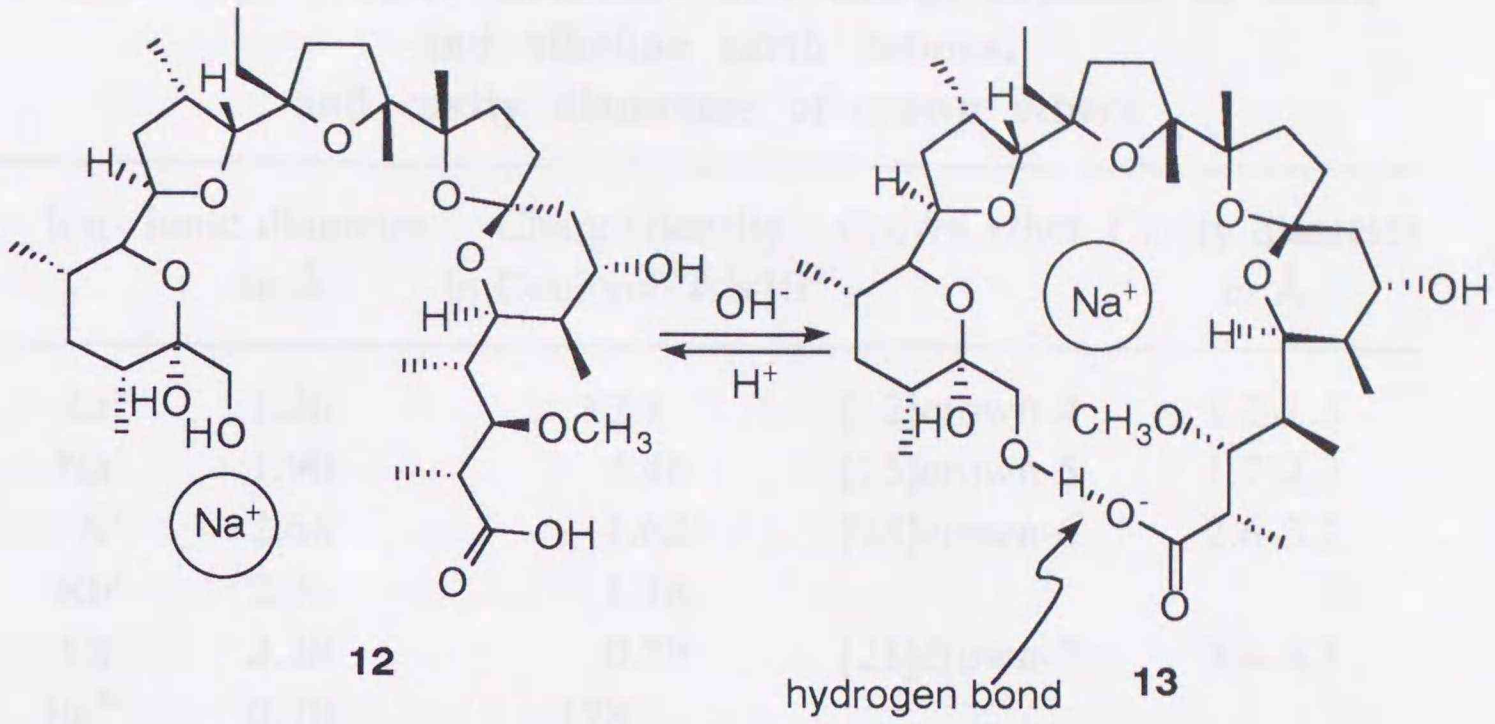
Valinomycin is a macrocyclic dodecadepsi-peptide with 12 subunits (α-amino and α-hydroxy-carboxylic acids) which are connected by alternate peptide and ester bonds, as shown in Scheme 1.5, and thereby is not able to adjust itself to cations of different radius. Whereas K^+ is of optimum size to fill the ligand cavity, Na^+ is too small to fully interact

Scheme 1.6



12 13

with all the ester oxygen. The exceptionally high K^+ / Na^+ discrimination displayed by valinomycin is unequaled by any other ionophore.

On the other hand, monensin **12** is a polyether antibiotic with a terminal carboxy group. The ion selectivities displayed by the polyether antibiotics are somewhat lower than those of macrocyclic ionophores, according to the structural features. In the complex, the monensin anion **13** is wrapped around the metal ion and held in the conformation as indicated in Scheme 1.6. The metal ion is entrapped in a hydrophilic cavity, while the exterior of the molecule is highly lipophilic thus fulfilling the requirements for an effective transmembrane transport. Monensin appears to be a good example to demonstrate how a biological host molecule utilizes a number of minor conformational changes in order to rearrange its binding sites for optimum complex formation with a guest entity.

Crown ethers, which are synthetic macrocyclic multidantates, are able to mimic effectively their natural counterpieces. Examination of the diameters of ligand cavities and of the diameters of alkali and alkaline earth ions, as given in Table 1.1[17], clearly shows that either the metal ions too small to fill the cavity, or too large to fit in it, or it just meets the cavity size. [12]Crown-4 and Li^+, [15]crown-5 and Na^+, and [18]crown-6 and K^+ are well matched. Because of their ability to take up ions and to transfer them across a lipophilic medium, these types of ligands also are

Table 1.1. Ionic diameters and charge densities of alkali and alkaline earth cations, and cavity diameters of crown ethers

Ion	Ionic diameter in Å	Charge density in Coulomb/Å^{3}x10^{20}	Crown ether	Cavity diameter in Å
Li^+	1.36	12.1	[12]crown-4	1.2-1.5
Na^+	1.90	4.46	[15]crown-5	1.7-2.2
K^+	2.66	1.62	[18]crown-6	2.6-3.2
Rb^+	2.96	1.18		
Cs^+	3.38	0.79	[21]crown-7	3.4-4.3
Be^{2+}	0.70	178		
Mg^{2+}	1.32	26.8		
Ca^{2+}	1.98	7.90		
Sr^{2+}	2.24	5.46		
Ba^{2+}	2.68	3.17		

ionophores.

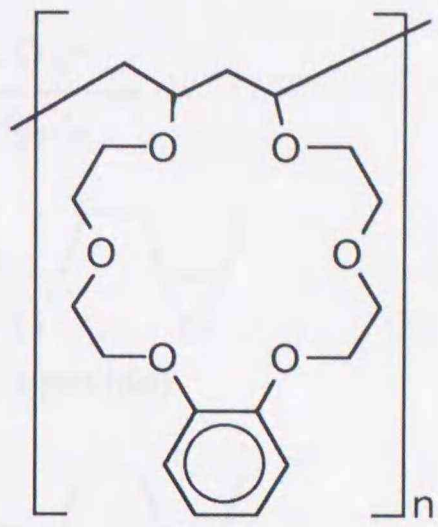
Polymeric crown ethers also act as an ionophore. Synthesis of macromolecular ionophore, however, has been limited to the incorporation of crown ether units into the polymer and little attention has been given to the synthesis of the polyether ionophores consisting of tetrahydrofuran and tetrahydropyran rings. Therefore, this subject has become of interest.

1.4 Object and Outline of the Thesis

Generally speaking, the cyclopolymerization tendency of nonconjugated dienes falls sharply for rings of more than six atoms. Therefore, the cyclopolymerization forming the polymer with medium and large rings need to be devised the design and synthesis of dienes. An effective technique was presented by Yokota and his co-workers.[26] The addition of alkylaluminium chlorides to the diene containing electropositive and negative double bonds, namely, 2-allylphenyl acrylate, caused a great

increase in the cyclopolymerization tendency. This technique was extended to the cyclopolymerization of higher homologues of 2-allylphenyl acrylate, which produced polymers with cyclic units up to 20-membered rings. The polymerization which forms rings and polymer chains at the same time was a practical method for preparing polymers with macrocyclic crown units such as benzo[16]crown-5, benzo[19]crown-6 **14**, and benzo-monothia[16]-crown-5 units from divinyl ethers.

Scheme 1.7



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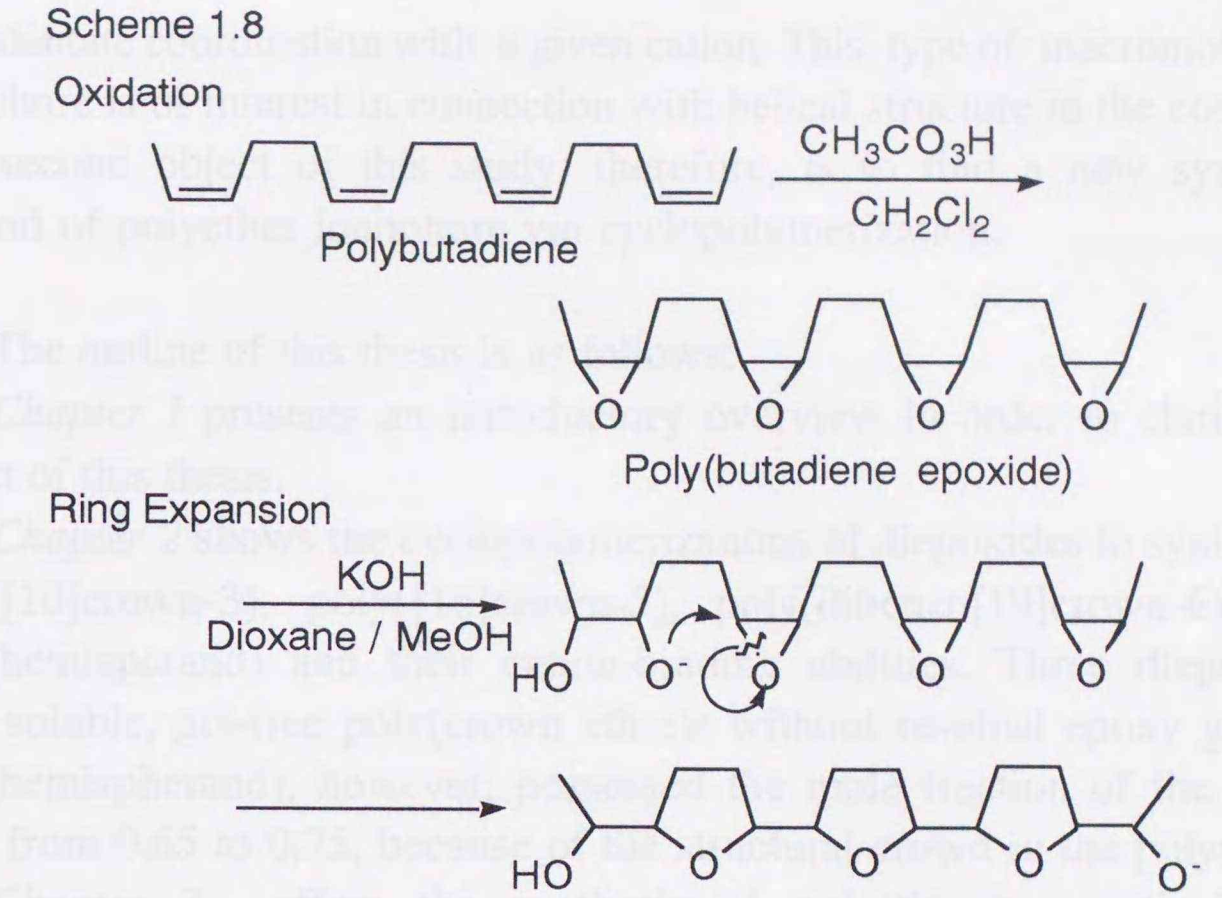
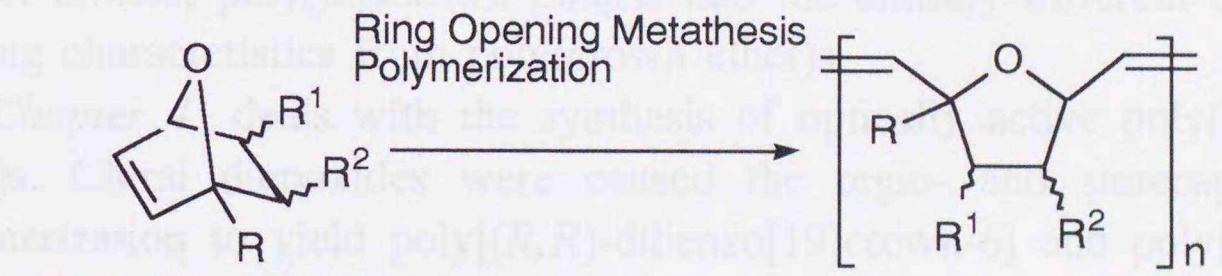
Thus, cyclopolymerization of diepoxy compounds should be a useful method of synthesizing poly(crown ether)s with ether linkages also in the polymer backbone. Several reports have been published on the cyclopolymerization of diepoxy compounds such as 1,2-bis(epoxyethyl)benzene, 1,2,4,5-diepoxypentane, 1,2,5,6-diepoxyhexane, and *N,N*-bis(2,3-epoxypropyl)aniline. They are concerned with the formation of rings containing five to seven ring atoms. Until recently, however, little attention was given to macroring formation from diepoxy compounds. The first object of this study, therefore, is to attain a new development in the cyclopolymerization of diepoxide and related compounds and thereby in the synthesis of polymeric crown ethers.

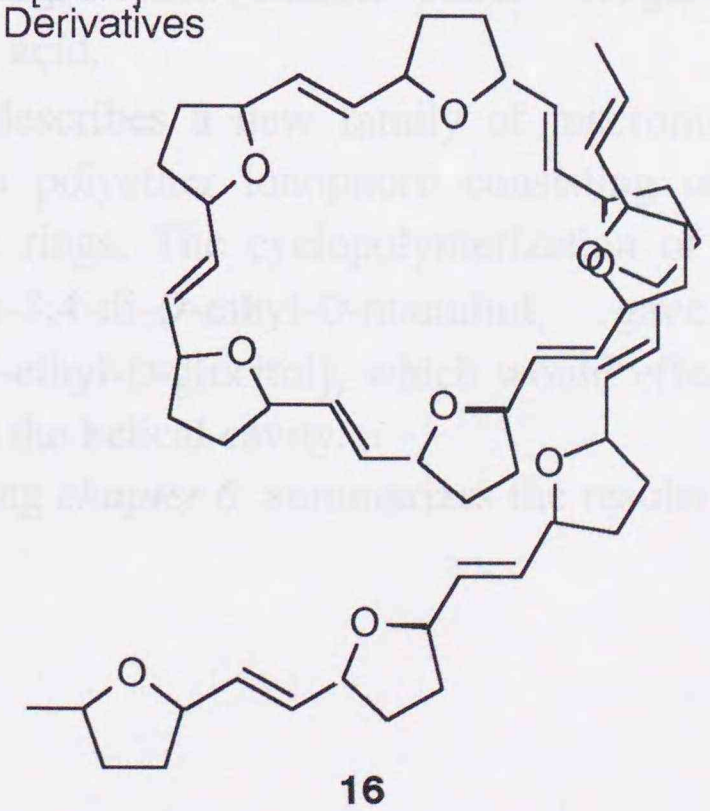
Synthetic macromolecular ionophore is limited to the type of crown ether. The ionophore belonging to the type of polyether can be found only in two reports. α,ω–Poly(cyclooxalkanediyl), the first synthetic polyether ionophore, was synthesized through the ring expansion of the oxiranes derived from the polymers of butadiene and cyclopentene by Smith et al.[27] The obtained *threo*-α,ω–poly(2,6-tetrahydrofuran)diyl **15** possessed the binding ability with cations, e.g., Li^+, Ba^{2+}, and methylene blue (Scheme 1.8). In addition, Grubbs et al.[28] have reported that poly(7-oxanorbornene) **16** resulting from the metathesis polymerization binds various cations containing methylene blue and rhodamine 6G (Scheme 1.9). Unlike the crown ethers, these acyclic ionophores form helical conformers capable of varying their pitch and cavity size to optimize

Scheme 1.8



Scheme 1.9





16

multidentate coordination with a given cation. This type of macromolecular ionophore is of interest in connection with helical structure in the complex. The second object of this study, therefore, is to find a new synthetic method of polyether ionophore via cyclopolymerization.

The outline of this thesis is as follows:

Chapter 1 presents an introductory overview in order to clarify the object of this thesis.

Chapter 2 shows the cyclopolymerizations of diepoxides to synthesize poly([10]crown-3), poly([16]crown-5), poly(dibenzo[19]crown-6), and poly(hemisperand) and their cation-binding abilities. Three diepoxides gave soluble, gel-free poly(crown ether)s without residual epoxy groups. Poly(hemispherand), however, possessed the mole fraction of the cyclic units from 0.65 to 0.75, because of the structural crowd in the polymer.

Chapter 3 offers the synthesis of poly(thiacrown ether)s via cyclopolymerization of diepisulfides. Because sulfides are characterized as soft donors, poly(thiacrown ether)s had the entirely different cation-binding characteristics from poly(crown ether)s.

Chapter 4 deals with the synthesis of optically active poly(crown ether)s. Chiral diepoxides were caused the regio- and stereospecific polymerization to yield poly[(*R,R*)-dibenzo[19]crown-6] and poly[(*S,S*)-dibenzo[19]crown-6], which exhibit chiral recognition ability toward racemic α–amino acid.

Chapter 5 describes a new family of macromolecular ionophores which belongs to polyether ionophore consisting of a linear array of tetrahydrofuranyl rings. The cyclopolymerization of diepoxide, namely, 1,2:5,6-dianhydro-3,4-di-*O*-ethyl-D-mannitol, gave poly[(1→6)-2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol], which would effectively bind various sizes of cations in the helical cavity.

The concluding *chapter 6* summarizes the results in this study.

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2

Syntheses of Polymers with Crown Ether and Hemispherand Units via Cyclopolymerization of Diepoxides

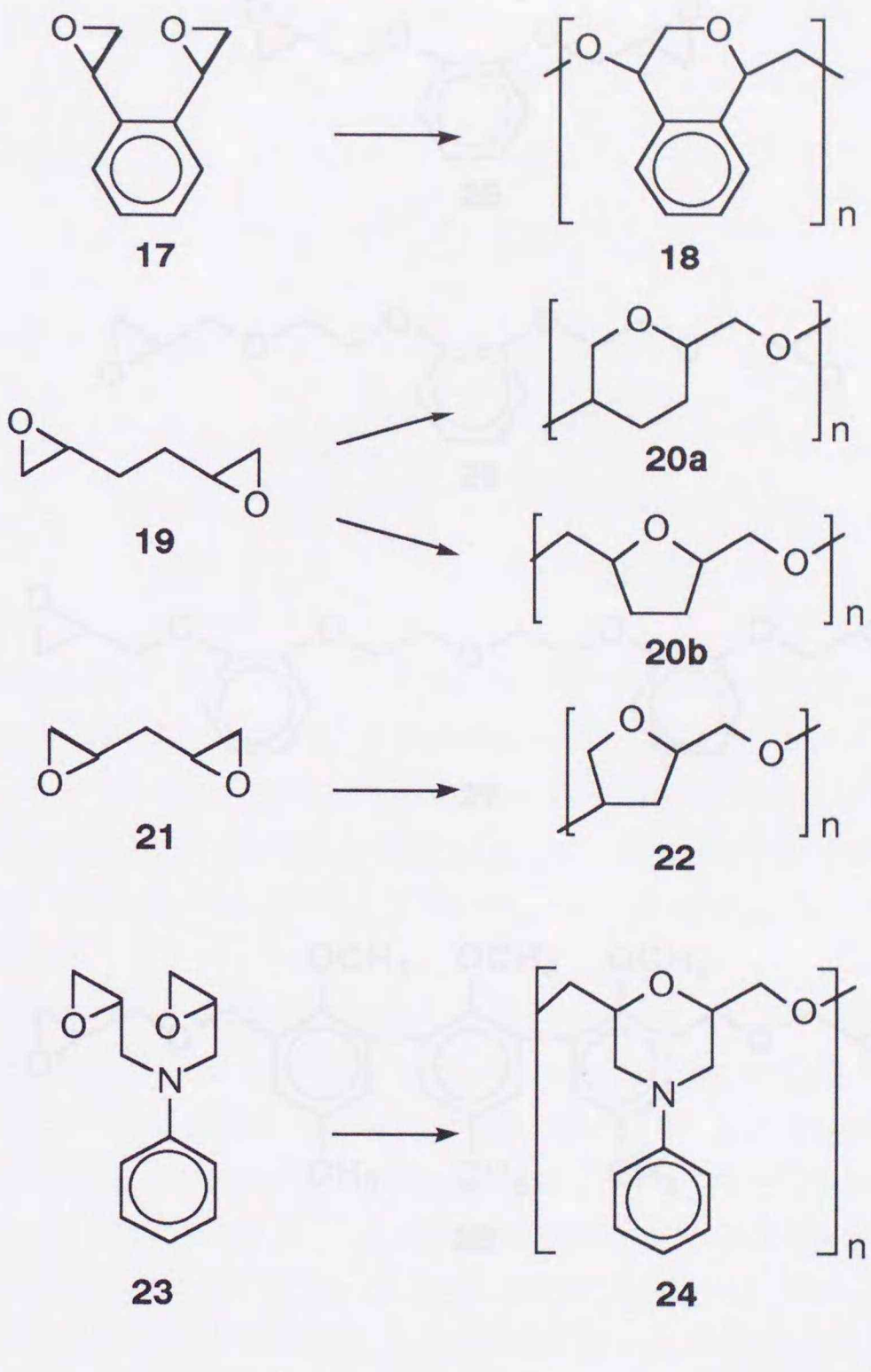
Crown ether units have been introduced into the polymer chain by various methods.[1] Since cyclopolymerizations form rings and polymer chain at the same time, polymers with crown ether units are readily prepared by means of an appropriate molecular design. Yokota and his co-worker[2] have synthesized the polymer with benzo[19]crown-6 **14** units via cyclopolymerization of divinyl ether. Thus, the cyclopolymerization of diepoxy compounds should be a facile method of synthesizing poly(crown ether)s with ether linkages also in the polymer backbone. This chapter describes the syntheses of poly(crown ether)s and poly(hemispherand) using cyclopolymerization of diepoxides and their cation-binding properties of resulting polymers.

2.1 Cyclopolymerization of Diepoxides

Several reports have been published on the cyclopolymerization of diepoxy compounds. Aso and his co-worker[3] reported on the polymerization of 1,2-bis(epoxyethyl)benzene **17** and 1,2:5,6-diepoxyhexane **19**. The properties of polymers **18** and **20a** suggested the polymerization mechanism to yield soluble polyethers with tetrahydrofuran recurring units, as shown in Scheme 2.1. Still et al.[4,5] also was obtained the similar results on the polymerizations of 1,2:5,6-diepoxyhexane **19** and 1,2:4,5-diepoxypentane **21**. Bauer[6] have proposed that *N,N*-bis(2,3-epoxypropyl)aniline **23** undergoes cyclopolymerization to give soluble polymers containing 2,4,6-substituted morpholindiyl units (polymer **24**) using potassium *t*-butoxide as initiator.

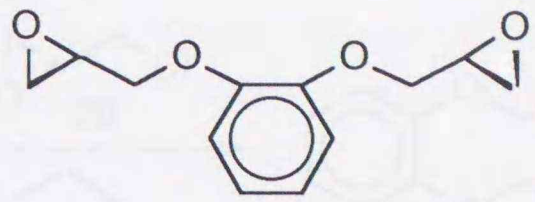
They are concerned with the formation of rings containing five to seven ring atoms. Until recently, however, little attention was given to macrocycles formation from diepoxy compounds. This chapter described the cyclopolymerizations of 1,2-bis(2,3-epoxypropoxy)benzene **25**,

Scheme 2.1



1,2-bis[2-(2,3-epoxypropoxy)ethoxy]benzene **26**, 5,6:14,15-dibenzo-1,2:18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene **27**, and 2,6-bis [3- (4,5- epoxy- 2- oxapentyl)- 2-methoxy-5-methylphenyl]-4-methyl-anisole **28** capable of forming 10-21-membered rings, as shown in Scheme 2.2, and the cation-binding characteristics of the resulting poly(crown ether)s and poly(hemispherand).

Scheme 2.2



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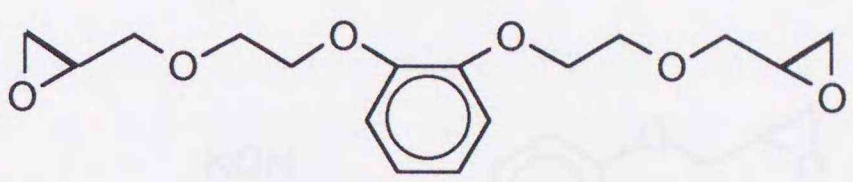

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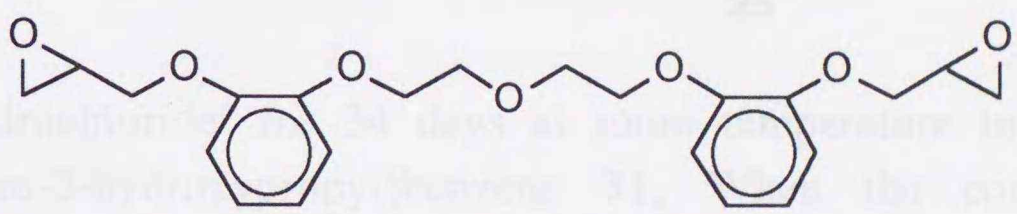

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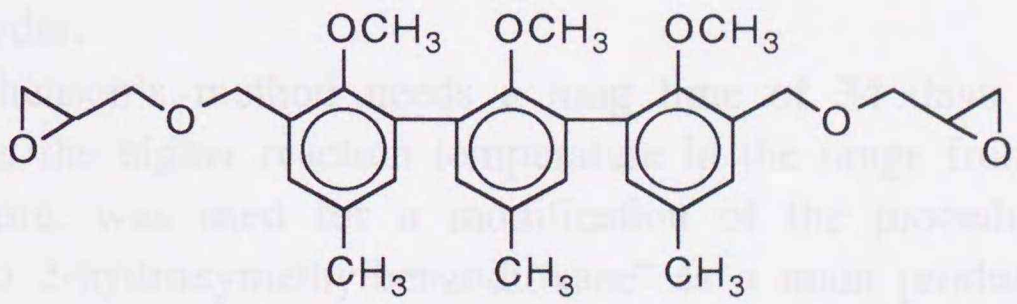


28

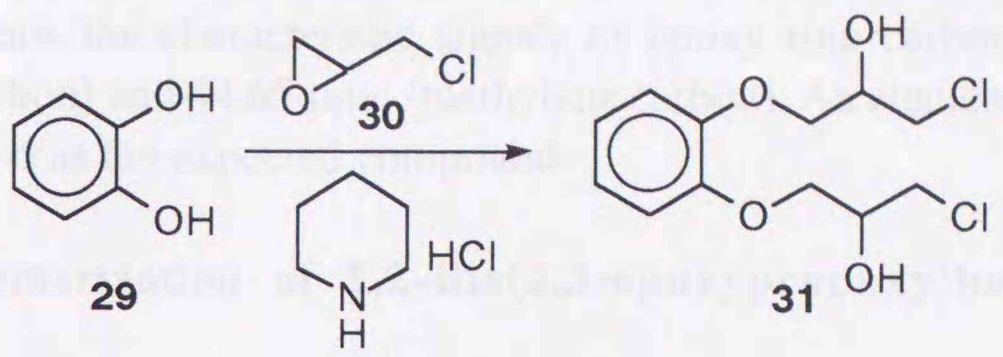
2.2 Synthesis of Poly([10]crown-3)

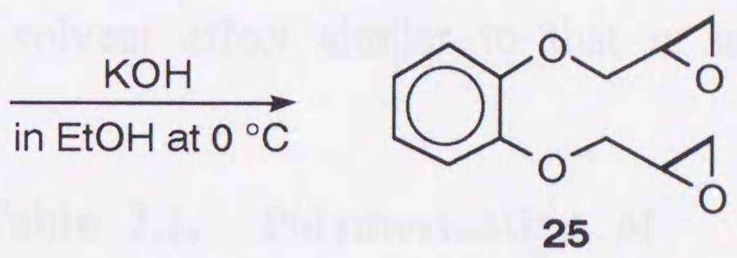
2.2.1 Preparation of 1,2-Bis(2,3-epoxypropoxy)benzene

1,2-Bis(2,3-epoxypropoxy)benzene **25** was prepared according to the procedure reported by Stepheson[7], as shown in Scheme 2.3.

1,2-Benzenediol (catechol) **29** was reacted with 1-chloro-2,3-epoxypropane (epichlorohydrin) **30** in the presence of

Scheme 2.3





piperidine hydrochloride[8] for 34 days at room temperature to obtain 1,2-bis(3-chloro-2-hydroxypropyl)benzene **31**. When the compound obtained was treated with potassium hydroxide in absolute ethanol at 0 °C, condensation of the hydroxyl group with the chloride was accompanied by ring closure, thereby producing 1,2-bis(2,3-epoxypropoxy)benzene **25** as a white powder.

The Stephenson's method needs a long time of 34 days for the reaction. When the higher reaction temperature in the range from 70 to 90 °C, therefore, was used for a modification of the procedure, the reaction led to 2-hydroxymethylbenzodioxane[9] as a main product. This compound was formed from 2-(2,3-epoxypropoxy)phenol that is a mono-substituted intermediate of **29**. The phenolic hydroxy and the epoxy groups easily react with each other, thus yielding a 1,4-dioxane derivative. Although being only 8% in the reaction at 100 °C, the yield of **31** increases to 90% for 40 days at room temperature, as indicated by Bartulin et al.[10] A minor product, 1,2-bis(2-hydroxy-3-ethoxypropoxy)benzene, was found by ring closure of **31** with potassium hydroxide in ethanol, resulting from an additional reaction of **25** with ethanol.

The IR spectrum of **25** showed the characteristic absorption bands corresponding to ring vibration of the epoxy group at 841 and 905 cm^{-1}. The ^{1}H NMR spectrum of **25** showed two double-doublet signals at 2.56

(1H) and 2.69 (1H) ppm assigned to the epoxy methylene protons and a multiplet one (3H) to the epoxy methine proton. The ^{13}C NMR spectrum of **25** presents the characteristic signals of epoxy ring carbons at 50.27 (methine carbon) and 44.65 ppm (methylene carbon). An elemental analysis was identified as the expected compound.

2.2.2 Polymerization of 1,2-Bis(2,3-epoxypropoxy)benzene

Some typical results of polymerization of **25** with Lewis acids are given in Table 2.1. A solvent effect similar to that in usual cationic

Table 2.1. Polymerization of 1,2-bis(2,3-epoxypropoxy)benzene with Lewis acids[a]

Initiator	Solvent	[Monomer] / [Initiator] in molar ratio	Time in h	Yield in %
$SnCl_4$	$C_2H_5NO_2$	20	0.17	58.1
$SnCl_4$	$ClCH_2CH_2Cl$	20	0.33	80.5
$SnCl_4$	CH_2Cl_2	20	0.33	65.5
$SnCl_4$	$C_6H_5CH_3$	20	0.17	38.4
$SnCl_4$	CH_2Cl_2	200	48	5.0
$BF_3 \cdot OEt_2$	CH_2Cl_2	200	48	57.0[b]
$BF_3 \cdot OEt_2$	CH_2Cl_2	20	48	70.6

[a] [Monomer]=0.5 mol•L^{-1}; temp, -30 °C.
[b] Extent of cyclization, f_c=68.6%.

polymerizations is found. The polymerization rate increases with increasing dielectric constant of solvents from toluene (ε=2.3807) to nitroethane (ε=28.06). In toluene and nitroethane, the polymerizations proceeded heterogeneously and the resulting polymers were partly soluble in chloroform and swelled in *p*-chlorophenol. The polymers obtained in 1,2-dichloroethane and dichloromethane were very soluble in chloroform. The ^1H NMR spectra of these polymers lost the absorption due to epoxy

function, but alternatively appeared those due to oxymethylene, as shown in Figure 2.1.

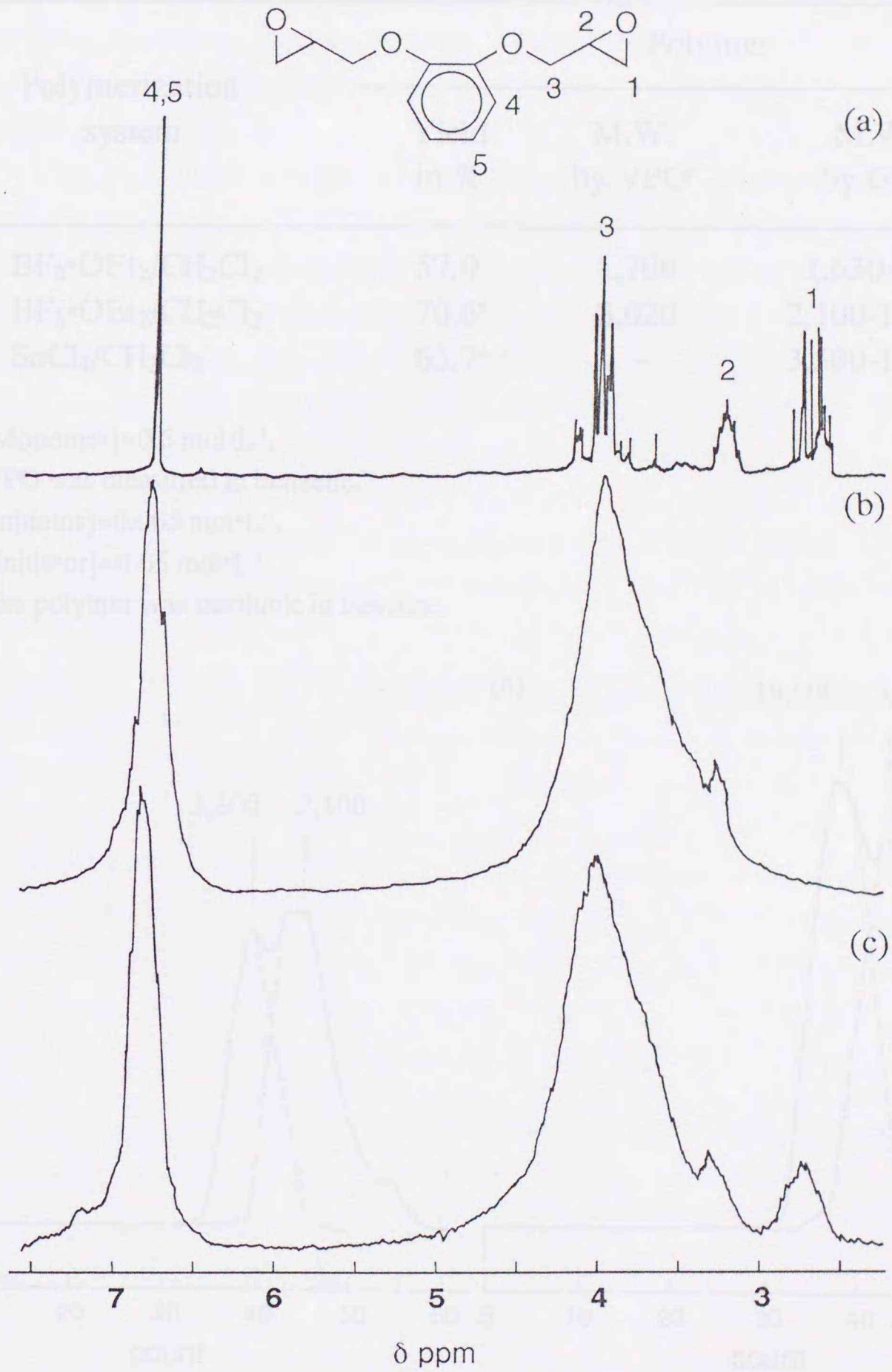


Figure 2.1. ^{1}H NMR spectra of (a) 1,2-(2,3-epoxypropoxy)-benzene 25 and polymers preparing with (b) $SnCl_4$ and (c) $BF_3 \cdot OEt_2$.

Table 2.2. Effect of reaction conditions on molecular weights of poly[1,2-bis(2,3-epoxypropoxy)benzene][a]

Polymerization system	Polymer		
	Yield in %	M.W. by VPO[b]	M.W. by GPC
BF_3•OEt_2/CH_2Cl_2	57.0[c]	1,700	1,630-1,750
BF_3•OEt_2/CH_2Cl_2	70.6[d]	3,020	2,100-11,500
$SnCl_4$/CH_2Cl_2	63.7[d, e]	-	3,500-19,000

[a] [Monomer]=0.5 mol•L^{-1}.
[b] VPO was measured in benzene.
[c] [Initiator]=0.005 mol•L^{-1}.
[d] [Initiator]=0.05 mol•L^{-1}.
[e] The polymer was insoluble in benzene.

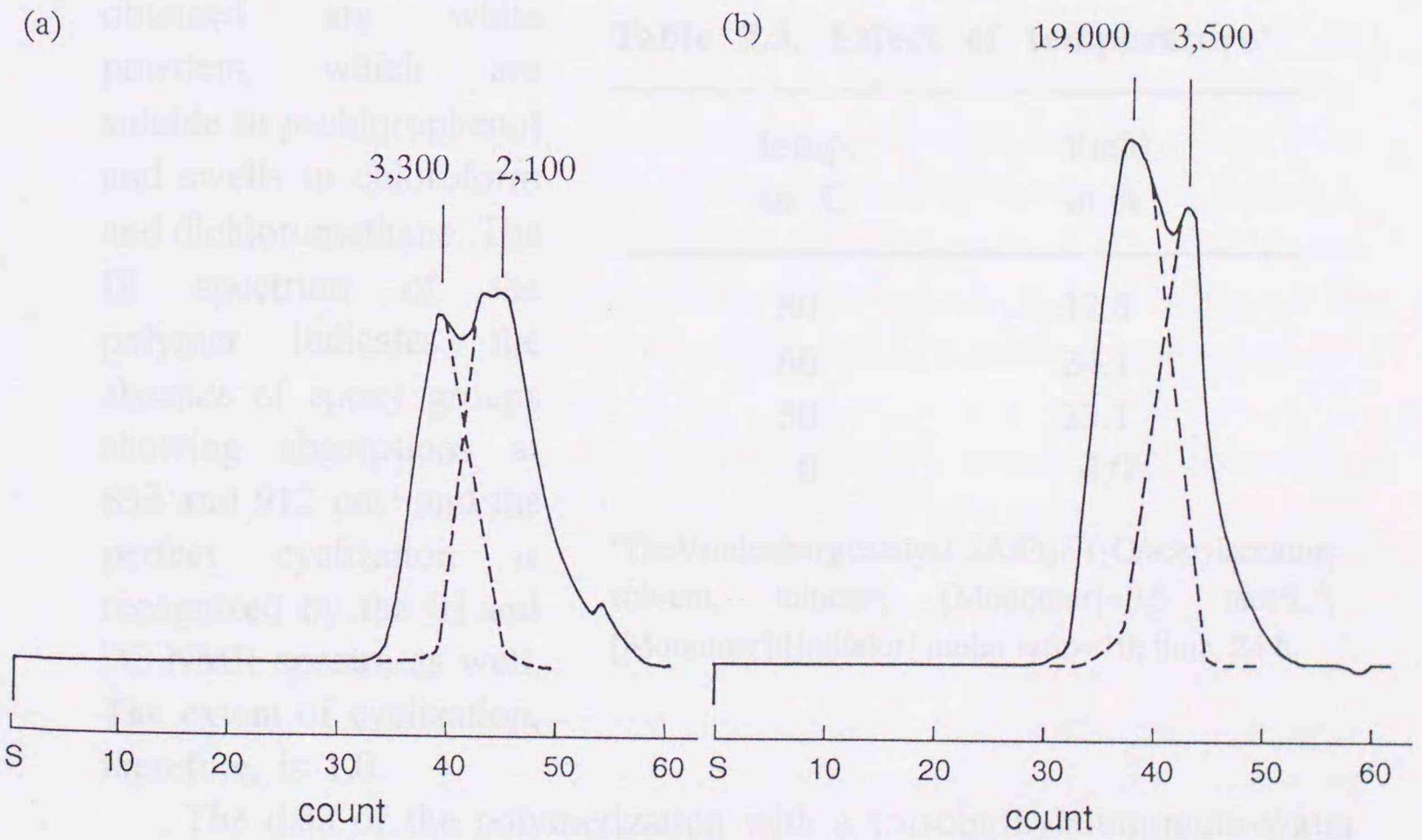


Figure 2.2. GPC profiles of the polymers obtained by (a) BF_3•OEt_2 / CH_2Cl_2 and (b) $SnCl_4$ / CH_2Cl_2 systems.

A variety of Lewis acids were used for polymerization. Aluminium bromide hardly occurred the polymerization. Boron trifluoride etherate was effective for the polymerization in homogeneous system. The polymer obtained possesses some residual epoxy functions and the extent of cyclization is 0.686 which was determined by the relative peak areas in the NMR spectrum.

The molecular weight of the polymers was estimated by a vapor pressure osmometry (VPO) and a gel permeation chromatography (GPC). Table 2.2 shows a satisfactory agreement in both measurements. All the polymers possess the molecular weight ranging from 1,600 to 3,000. The polymers obtained by BF_3•OEt_2 / CH_2Cl_2 and $SnCl_4$ / CH_2Cl_2 systems indicated the GPC profiles with bimodal distributions. The result shows a complicating feature in this polymerization.

The polymerization with Vandenberg[11] catalyst consisting of triethylaluminium, water, and acetylacetone (molar ratio 2/1/1) gave polymers only at the temperature more than 30 °C, as indicated in Table 2.3. The polymers obtained are white powders, which are soluble in *p*-chlorophenol and swells in chloroform and dichloromethane. The IR spectrum of the polymer indicates the absence of epoxy groups showing absorptions at 858 and 912 cm^{-1} and the perfect cyclization is recognized by the ^1H and ^{13}C NMR spectra as well. The extent of cyclization, therefore, is 1.0.

Table 2.3. Effect of temperature[a]

Temp. in °C	Yield in %
80	32.5
60	24.1
30	23.1
0	4.0

[a]The Vandenberg catalyst, $2AlEt_3/H_2O$/acetylacetone; solvent, toluene; [Monomer]=0.5 mol•L^{-1}; [Monomer]/[Initiator] molar ratio=10; time, 24 h.

The data of the polymerization with a triisobuthylaluminium-water catalyst was shown in Table 2.4. The polymerization system is homogeneous at 30 and 60 °C, but is heterogeneous at 0 °C.

Table 2.4. Polymerization of 1,2-bis(2,3-epoxypropoxy)benzene with Al(*i*-Bu)$_3$-H$_2$O catalyst[a]

Temp. in °C	Time in h	Yield in %
60	0.5	25.3
30	0.5	27.1
0	1.5	30.8

[a] [Monomer]=0.5 mol•L^{-1}; [Monomer] / [Initiator] molar ratio=10; solvent, toluene.

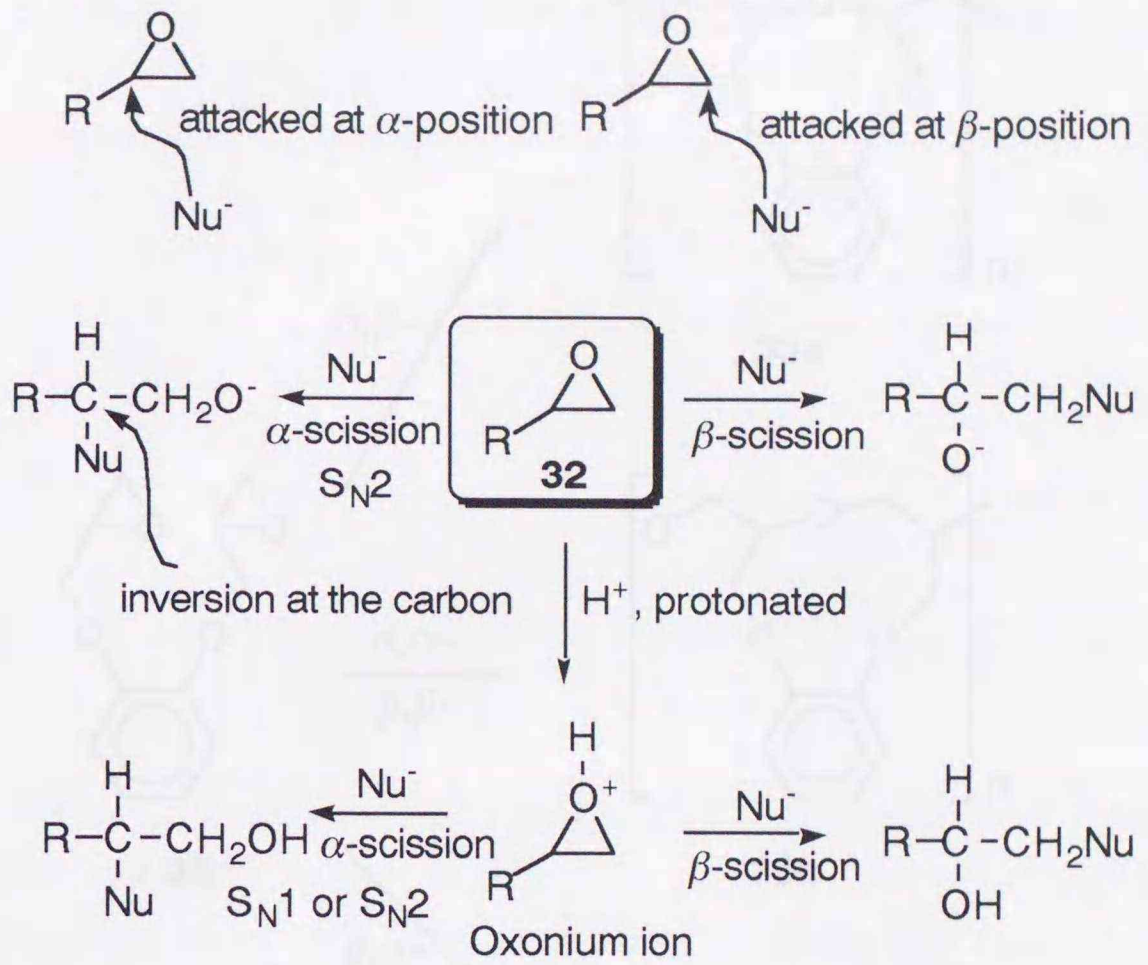
2.2.3 Structure of Poly([10]crown-3)

Illuminati et al.[12] have revealed that oxygen atom effects arising from the replacement of a methylene group with an oxygen atom are found to facilitate ring closure on the formation of aromatic ethers via intramolecular Williamson synthesis. A significant oxygen atom effect caused a cyclization reaction to occur more readily in the cyclopolymerizations of acrylates and methacrylates containing oligooxyethylene units in the 10- to 20-membered ring region.[13] Divinyl ethers having oxyethylene bonds led to the perfectly cyclized polymers consisting of 13- and 19-membered crown rings.[2,14]

The cyclopolymerization of diepoxide **25** consumed all the epoxy functions to form soluble and gel-free polymers even at high conversions as well.

1,2-Epoxide has one methylene group and one methine group susceptible to attack.[15] The methylene group has a higher reactivity toward nucleophilic attack than the methine group according to a S_N2 mechanism. The nucleophilic attack to β-position in compound **32** results in retention of configuration at the methine carbon, since attack on the higher substituted group at α-position is inhibited by the steric effects (Scheme 2.4). Under acidic conditions the reaction is considered to be S_N1 and/or S_N2 cleavage of the oxonium ion. The epoxides are randomly cleaved at α- and β-positions

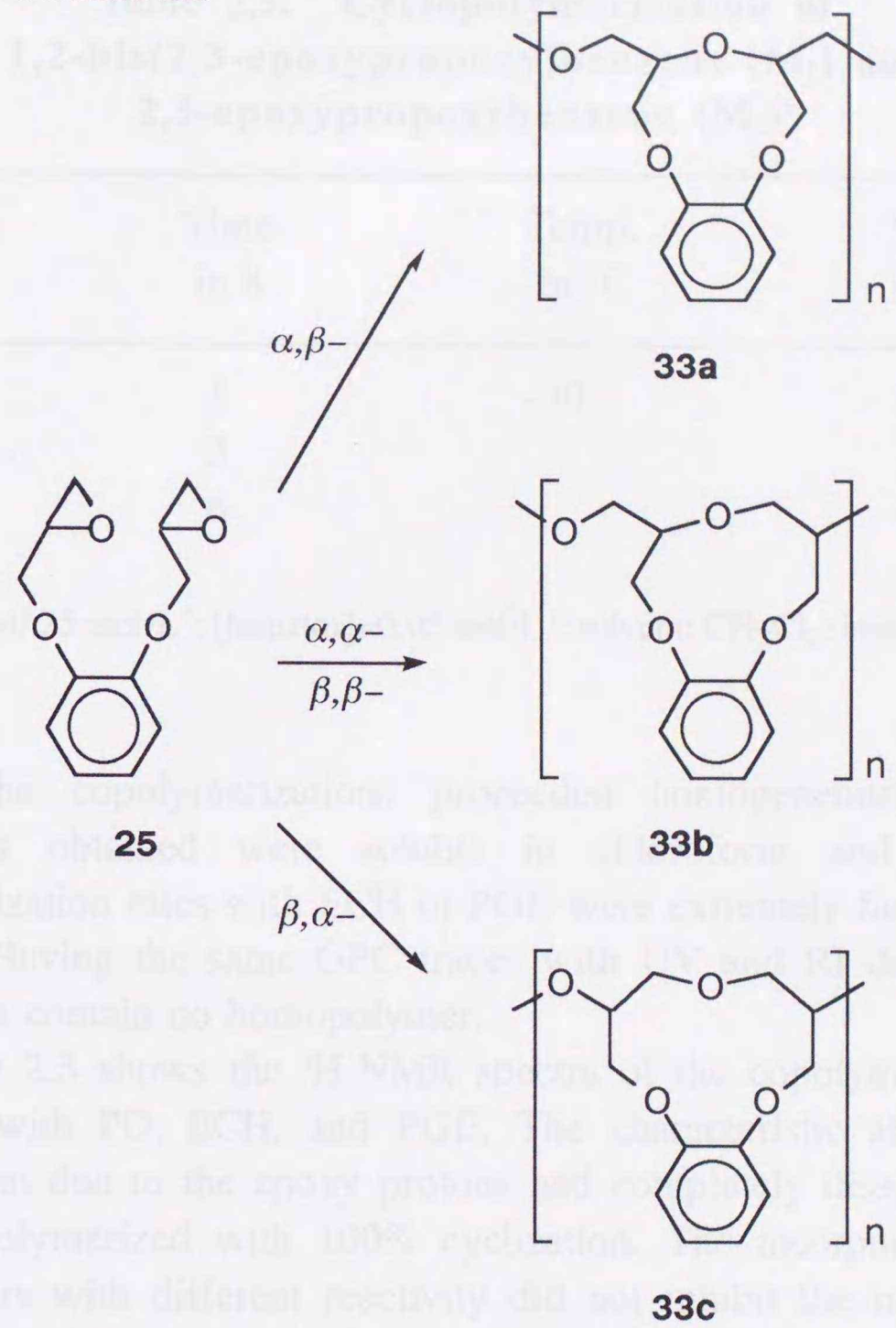
Scheme 2.4



by the S_N1 mechanism. The S_N2 cleavage occurs at the methine carbon with inversion of configuration. The acid-catalyzed polymerization, thus, is less selective in cleavage. These different modes in cleavage give rise to large differences in the polymer structure depending on the mode of initiation.

In the ring-opening polymerization of diepoxide **25**, the intramolecular cyclization due to α,α– and β,β–scissions may lead to form the polymers with 10-membered rings (polymer **33b**), whereas α,β- and β,α–scissions should induce the polymers with 9- and 10-membered rings (polymers **33a** and **c**) respectively, as shown in Scheme 2.5. Coordinate-type catalysts promote the polymerization of epoxides to give stereoregular polymers, resulting in β-scissions.[11,16] The polymer prepared with the Vandenberg catalyst, therefore, should essentially consist of 10-membered rings i.e. benzo[10]crown-3 units (polymer **33b**). The acid-catalyzed polymerizations induce α– and β–scissions[17], and the polymers obtained contain a mixture of three cyclic units.

Scheme 2.5



33a

25

33b

33c

2.2.4 Copolymerization of 1,2-Bis(2,3-epoxypropoxy)benzene with Monoepoxy Comonomers

The cationic copolymerizations of **25** with monoepoxy comonomers, propylene oxide (PO, **34**), epichlorohydrin (ECH, **30**), or phenyl glycidyl ether (PGE, **37**), were carried out with tin(Ⅳ) chloride in dichloromethane at -30 °C. Some results of the copolymerization are given in Table 2.5.

Table 2.5. Cyclopolymerization of 1,2-bis(2,3-epoxypropoxy)benzene (M_1) and 2,3-epoxypropoxybenzene (M_2)[a]

Run No.	Time in h	Temp. in °C	Yield in %
1	1	-30	54.0
2	3		71.7
3	6		68.2

[a] $[M_1]=[M_2]=0.25$ mol•L^{-1}; [Initiator]=0.05 mol•L^{-1}; solvent: CH_2Cl_2; initiator, $SnCl_4$.

All the copolymerizations proceeded homogeneously, and the copolymers obtained were soluble in chloroform and THF. The copolymerization rates with ECH or PGE were extremely faster than that with PO. Having the same GPC traces with UV and RI detections, the copolymers contain no homopolymer.

Figure 2.3 shows the ^{1}H NMR spectra of the copolymers obtained from **25** with PO, ECH, and PGE. The characteristic absorptions at 2.7-3.5 ppm due to the epoxy protons had completely disappeared, and thus **25** polymerized with 100% cyclization. The incorporation of the comonomers with different reactivity did not inhibit the intramolecular cyclization of **25**. The polymerization of monosubstituted epoxides with a cationic initiator proceeds through ring opening at the CH-O and CH_2-O bonds (α- and β-bonds).[17] For the cationic copolymerization of **25**, the main cyclic constitutional units in the copolymer is benzo[10]crown-3 (Scheme 2.6). The mole fraction of M_1 units in the copolymers, which were determined by ^{1}H NMR spectra, was 0.53 as a minimum value and increased in the order of PO < ECH < PGE.

Figure 2.4 shows the copolymer composition curve for the copolymerization of **25** and PGE with $SnCl_4$ in CH_2Cl_2 at -30 °C. The copolymerization reactivity ratios for **25** (M_1) and PGE (M_2) were estimated by use of the usual Mayo-Lewis equation and the Kelen-Tüdös method,

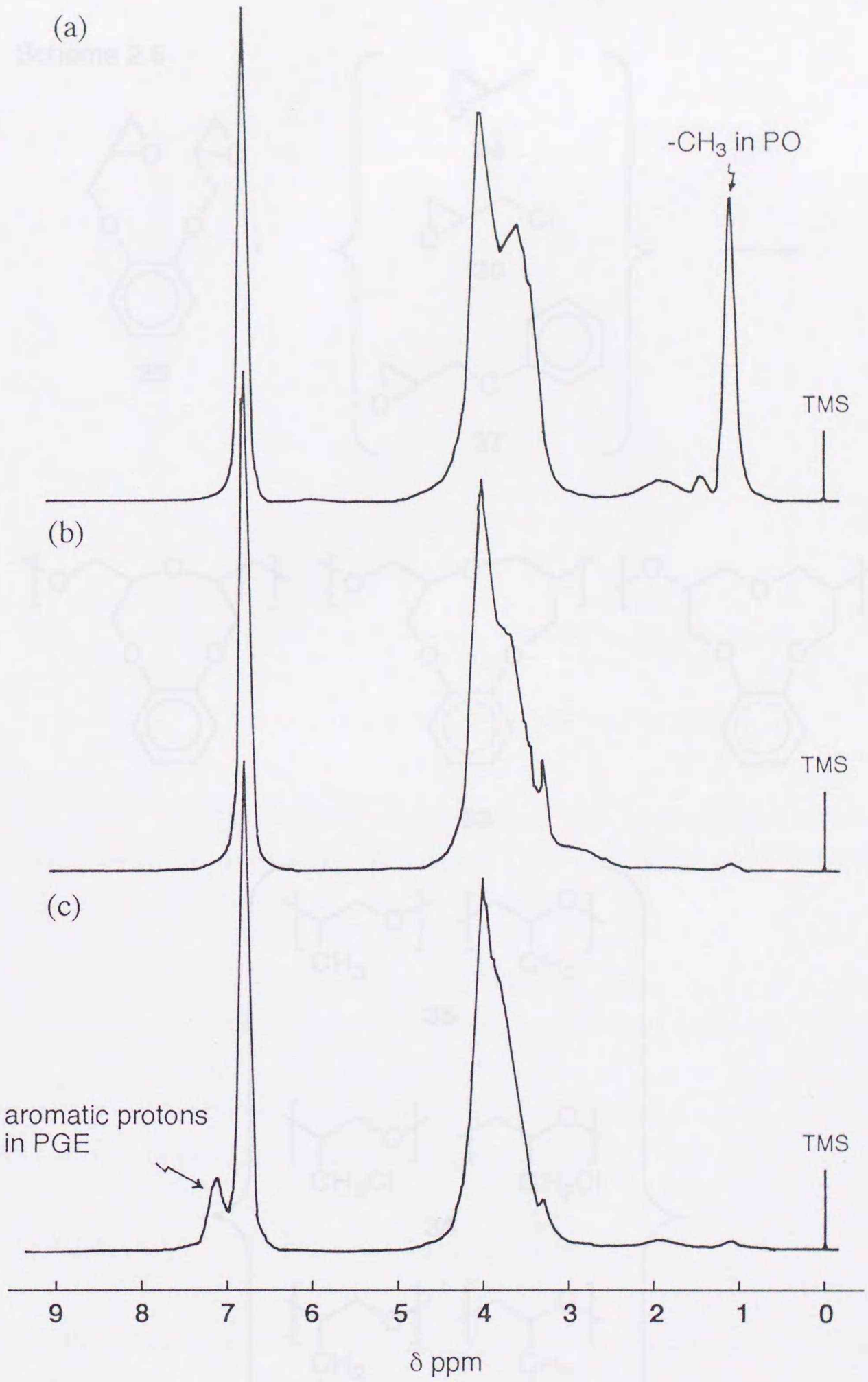
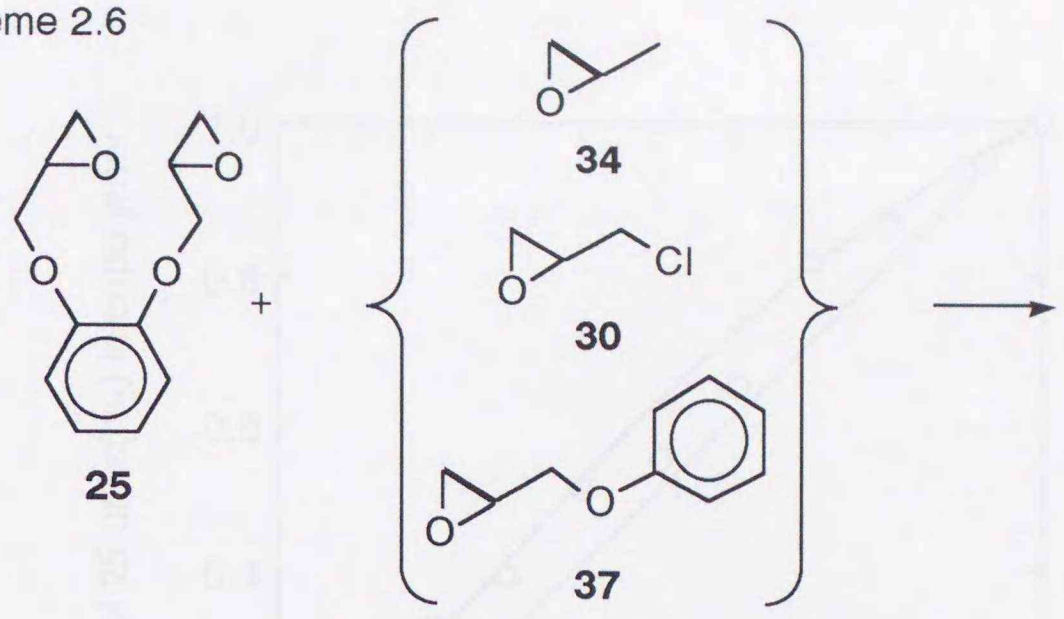
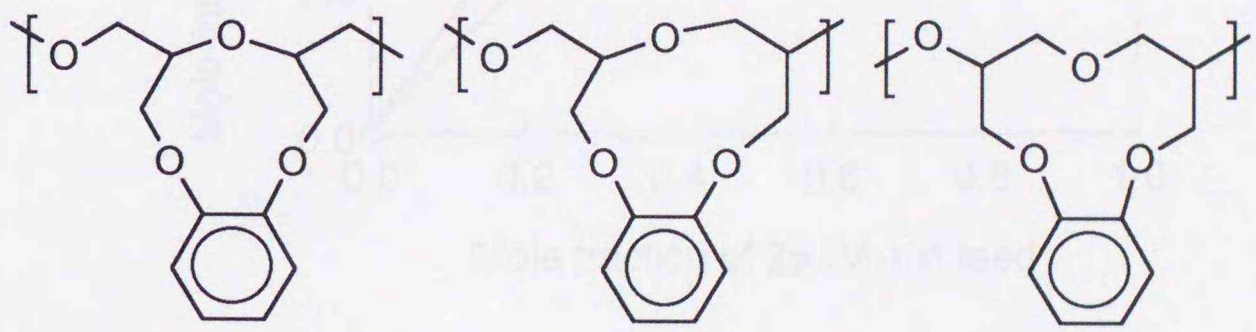


Figure 2.3. ^{1}H NMR spectra of (a) poly(25-*co*-PO), (b) poly(25-*co*-ECH), and (c) poly(25-*co*-PGE): [25] and [comonomer], 0.5 mol•L^{-1}; $SnCl_4$, 0.05 mol•L^{-1}; solvent, CH_2Cl_2; temp, -30 °C.

Scheme 2.6





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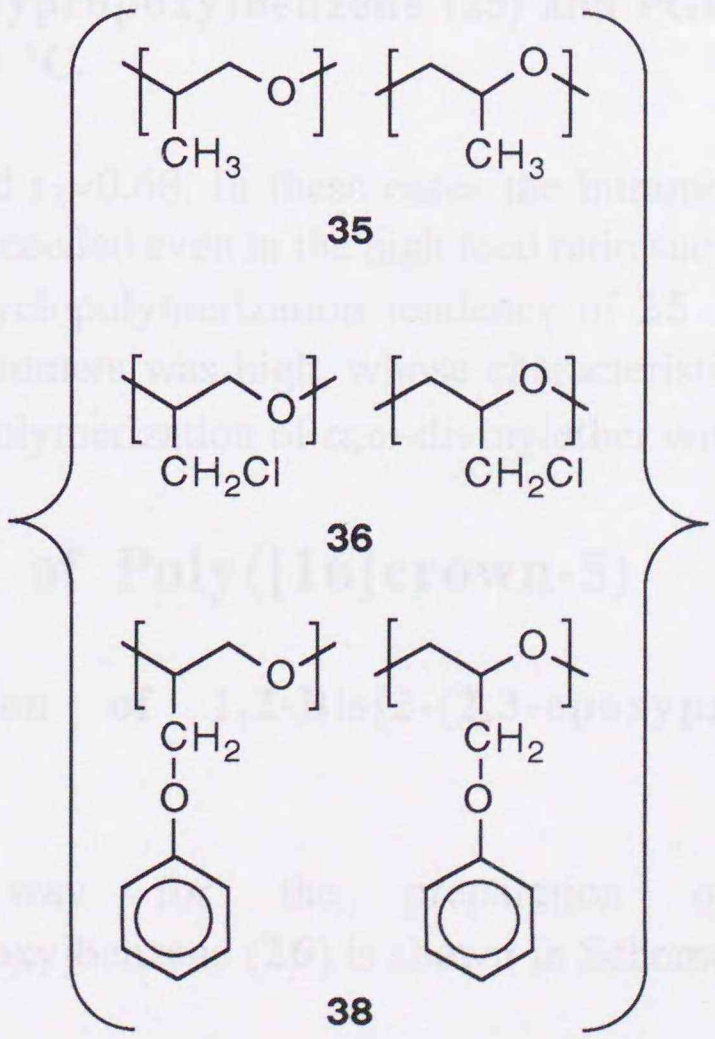


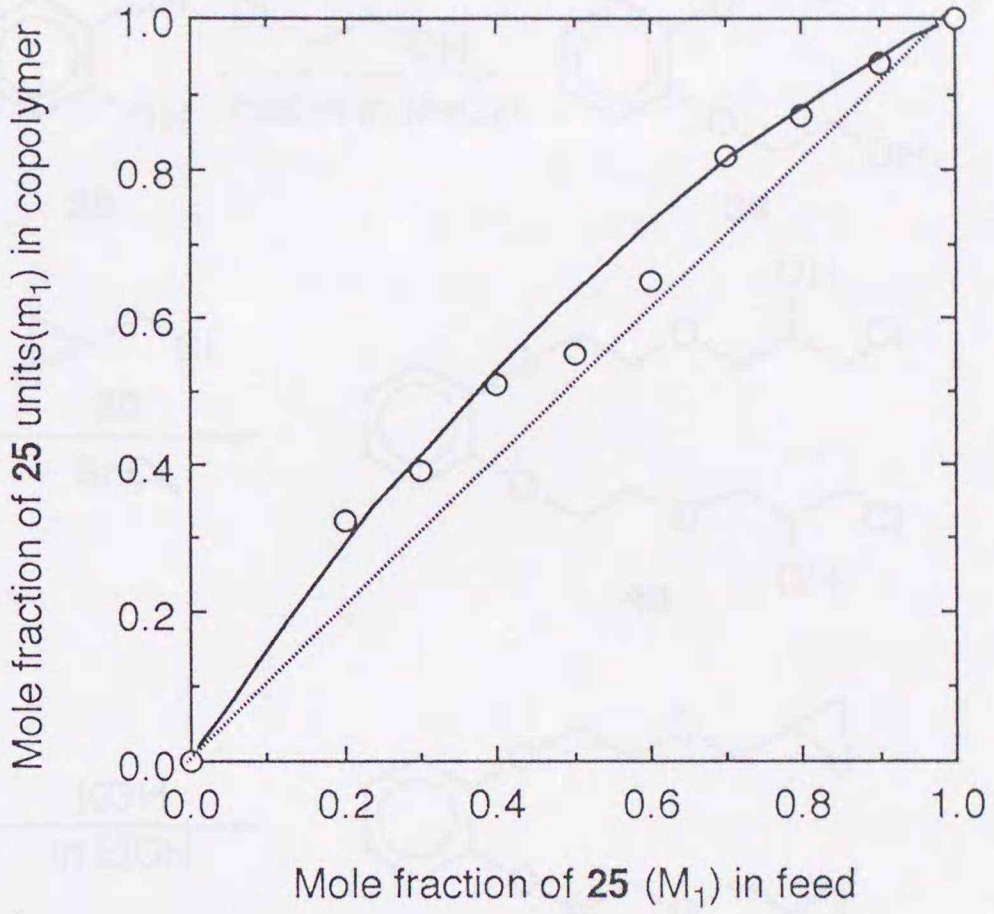


Figure 2.4. Composition curve for the copolymerization of 1,2-bis(2,3-epoxypropoxy)benzene (25) and PGE (37) with $SnCl_4$ in CH_2Cl_2 at -30 °C.

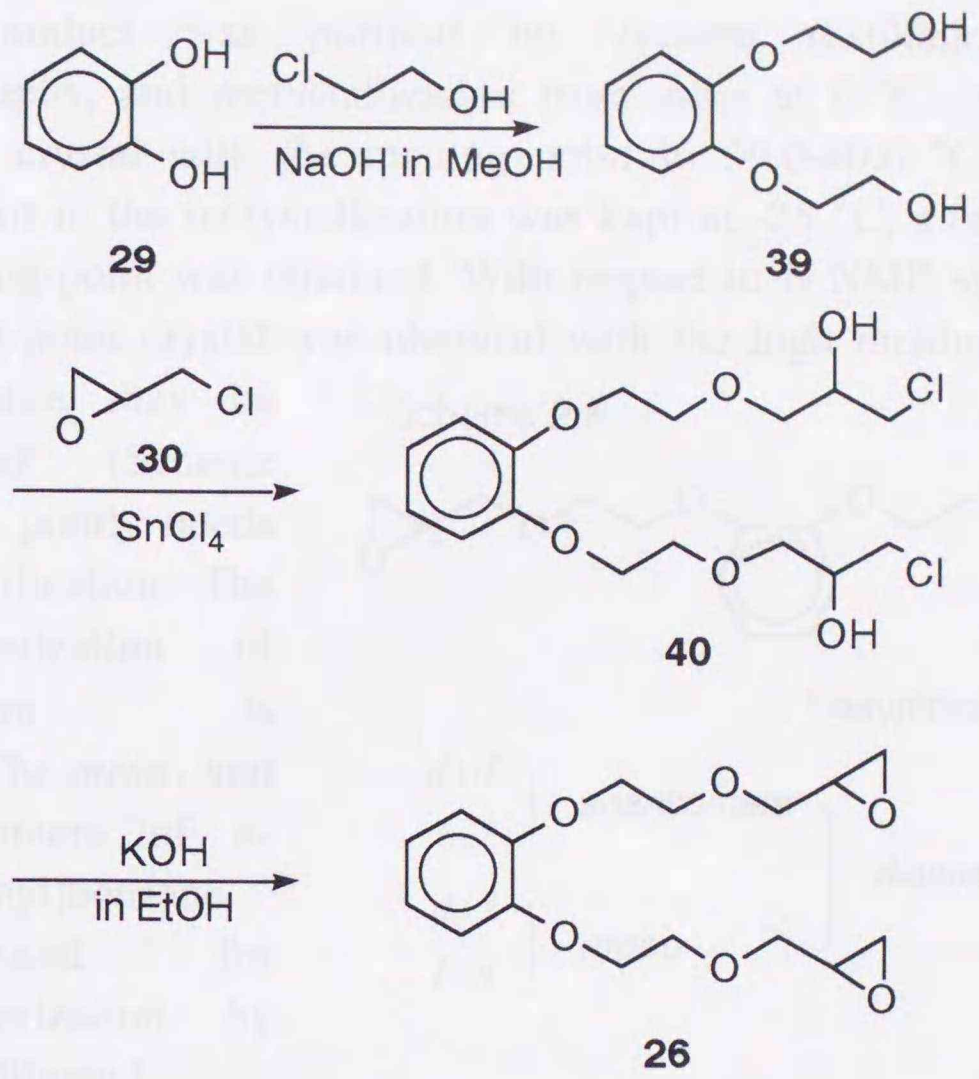
giving r_1=1.67 and r_2=0.68. In these cases the intramolecular cyclization of **25** perfectly proceeded even in the high feed ratio such as the [PGE]/[**25**] ratio of 4. The cyclopolymerization tendency of **25** in the presence of monoepoxy comonomers was high, whose characteristic was very similar to the cationic copolymerization of α,ω-divinylether with monovinylether.

2.3 Synthesis of Poly([16]crown-5)

2.3.1 Preparation of 1,2-Bis[2-(2,3-epoxypropoxy)ethoxy]-benzene

A path way for the preparation of 1,2-bis[2-(2,3-epoxypropoxy)ethoxy]benzene (**26**) is shown in Scheme 2.7.

Scheme 2.7

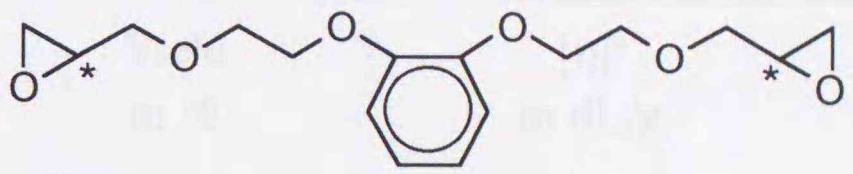


1,2-Benzenediol as a starting material reacted with 2-chloroethanol in alcoholic alkaline medium, giving 2,2'-(1,2-phenylenedioxy)diethanol (**39**).[18] The condensation of **39** with 1-chloro-2,3-epoxypropane was attended with ring opening of epoxy group to produce a bischlorohydrin (**40**).[19] By treatment with potassium hydroxide in absolute ethanol at 0 °C, **40** converted to **26** in 25% yield as a viscous liquid.[20] The IR spectrum of **26** showed characteristic absorption bands due to the epoxy group at 840 and 912 cm^{-1}. The ^{1}H NMR spectrum showed two double-doublet signals at 2.61 (2H) and 2.78 (2H) ppm and a multiplet signal at 3.19 (2H) ppm which are associated with the epoxymethylene and methine protons, respectively. The ^{13}C NMR spectrum found characteristic signals due to the epoxy methine and methylene carbons at 50.81 and 44.19 ppm, respectively. In the mass spectrometry, the molecular ion appeared at *m/e* 310 corresponding to the molecular weight of **26** and another ion at *m/e* 57 to the glycidyl group. The product was identified by elemental analysis as the expected diepoxide corresponding to the formula $C_{16}H_{22}O_6$

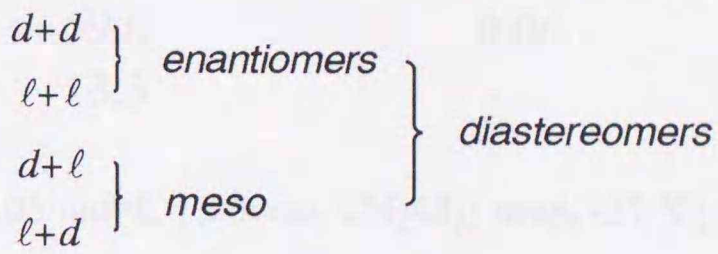
with an error less than 0.1.

The product was purified by vacuum distillation, column chromatography, and recrystallization from ether at 0 °C, affording **26** as a white crystal with the melting point to 39.0-40.6 °C. When the mother liquor in the recrystallization was kept at -25 °C, a crystal with a lower melting-point was obtained. With respect to ^{1}H NMR spectrum, the low melting-point crystal was identical with the high melting-point one. These crystals may be diastereomers (Scheme 2.8); this point needs further clarification. The cyclopolymerization of diastereomers is attractive. The *meso*- and *d,l*-diastereomers of *o*-bis(epoxyethyl)benzene were used for cyclopolymerization by Stille and Hillman.[5]

Scheme 2.8



* asymmetric carbon



2.3.2 Polymerization of 1,2-Bis[2-(2,3-epoxypropoxy)-ethoxy]benzene

The polymerization of **26** was carried out using the high melting-point crystal. Some typical results are given in Table 2.6. The polymerization of **26** was slower than that of **25**. The polymer was quantitatively obtained by the polymerization in nitroethane, and given a yield of 78% in toluene. The decreasing order of activity of the cationic initiators is as follows: $SnCl_4$ > BF_3 > $AlBr_3$. The polymers were colorless gummy, soluble in benzene dichloromethane, and chloroform. The number-average molecular weight ($\overline{M}_n$) was 3,300 corresponding to the degree of polymerization from 10 to 11, when measured by use of a vapor pressure osmometer in benzene.

In the presence of the Vandenberg catalyst, the polymer obtained was a white solid, insoluble in dichloromethane and chloroform, and soluble only in *p*-chlorophenol. The polymer is sparingly soluble; this is attributable

to higher molecular weight, as seen in the specific viscosity η_{sp}/c=0.59 dL/g which is higher than 0.06 dL/g for the polymer obtained with the Lewis acid. The Vandenberg catalyst is effective in preparing polymers of high molecular weight (Table 2.7).

Table 2.6. Polymerization of 1,2-bis[2-(2,3-epoxypropoxy)ethoxy]benzene with Lewis acid[a]

Initiator	Yield in %	$[\eta]$[b] in dL/g
$SnCl_4$	78.0	0.06[c]
$BF_3 \cdot OEt_2$	59.6	0.06
$AlBr_3$	13.3	-

[a] [Monomer]=0.5 mol•L^{-1}; [Initiator]=0.05 mol•L^{-1}; solvent, CH_2Cl_2; temp, -27 °C; time, 48 h.

[b] Measured in *p*-chlorophenol at 50 °C.

[c] The number-average molecular weight ($\overline{M}_n$) was 3,300 by means of a vapour pressure osmometer in benzene, which corresponds to the degree of polymerization of 10-11.

Table 2.7. Polymerization of 1,2-bis[2-(2,3-epoxypropoxy)ethoxy]benzene with the Vandenberg catalyst[a]

Temp. in °C	Time in h	Yield in %	$[\eta]$[b] in dL/g
30	24	8.9	-
60	2	22.6	0.40
80	2	55.6	0.59

[a] Initiator, $AlEt_3$ / H_2O / acetylacetone, mole ratio 2:1:1; [Monomer]=0.5 mol•L^{-1}; [Initiator]=0.05 mol•L^{-1}; solvent, toluene.

[b] Measured in *p*-chlorophenol at 50 °C.

Both the polymers obtained with cationic and coordination catalysts showed the IR spectra which have no absorption due to the epoxy group at 858 and 912 cm^{-1}. The ^{1}H and ^{13}C spectra also gave the similar results. Figure 2.5 shows the ^{1}H NMR spectra of **26** and the polymers prepared with tin(Ⅳ) chloride and the Vandenberg catalysts. According as the

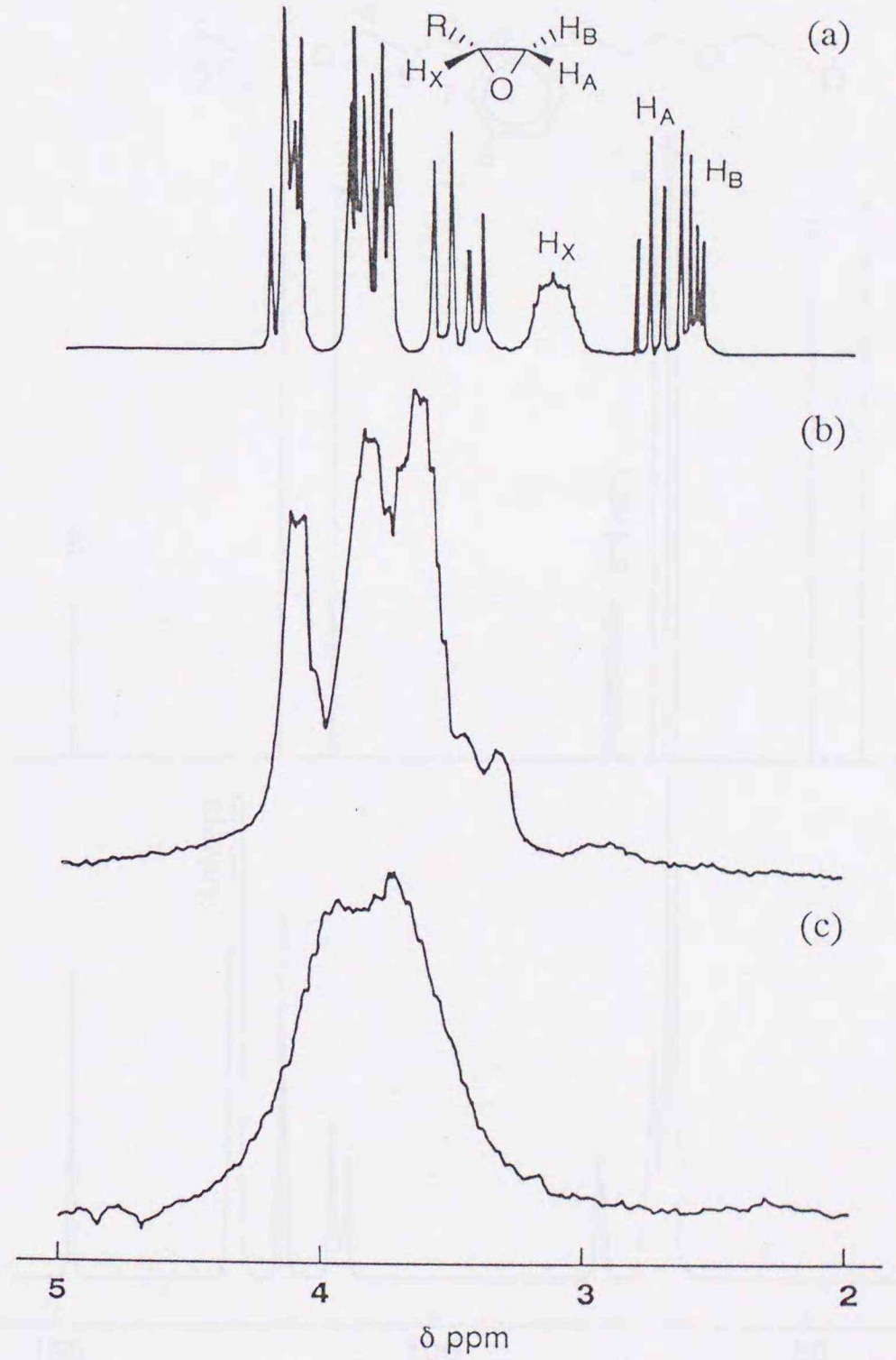


Figure 2.5. Partial ^{1}H NMR spectra of (a) 1,2-bis[2-(2,3-epoxypropoxy)ethoxy]benzene 26 and the polymers preparing with (b) $SnCl_4$ and (c) the Vandenberg catalysts.

progress of polymerization, the characteristic resonances at 2.62, 2.78, and 3.19 ppm, due to the methylene and the methine protons of the epoxide, disappeared together with an alternative appearance of the resonances at 3.6 ppm due to the oxymethylene protons. Figure 2.6 shows the ^{13}C NMR spectra of **26** and the polymer prepared by cationic

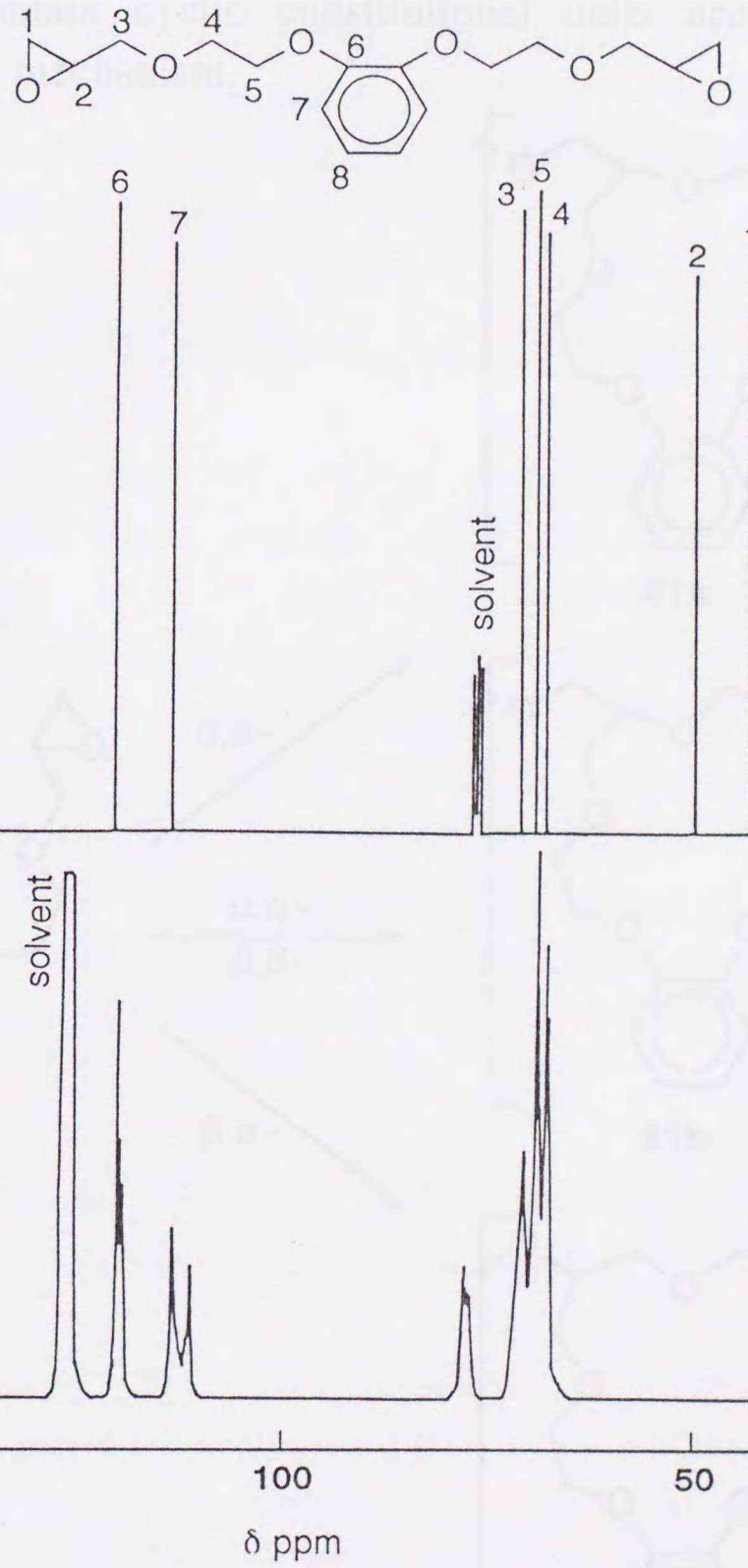
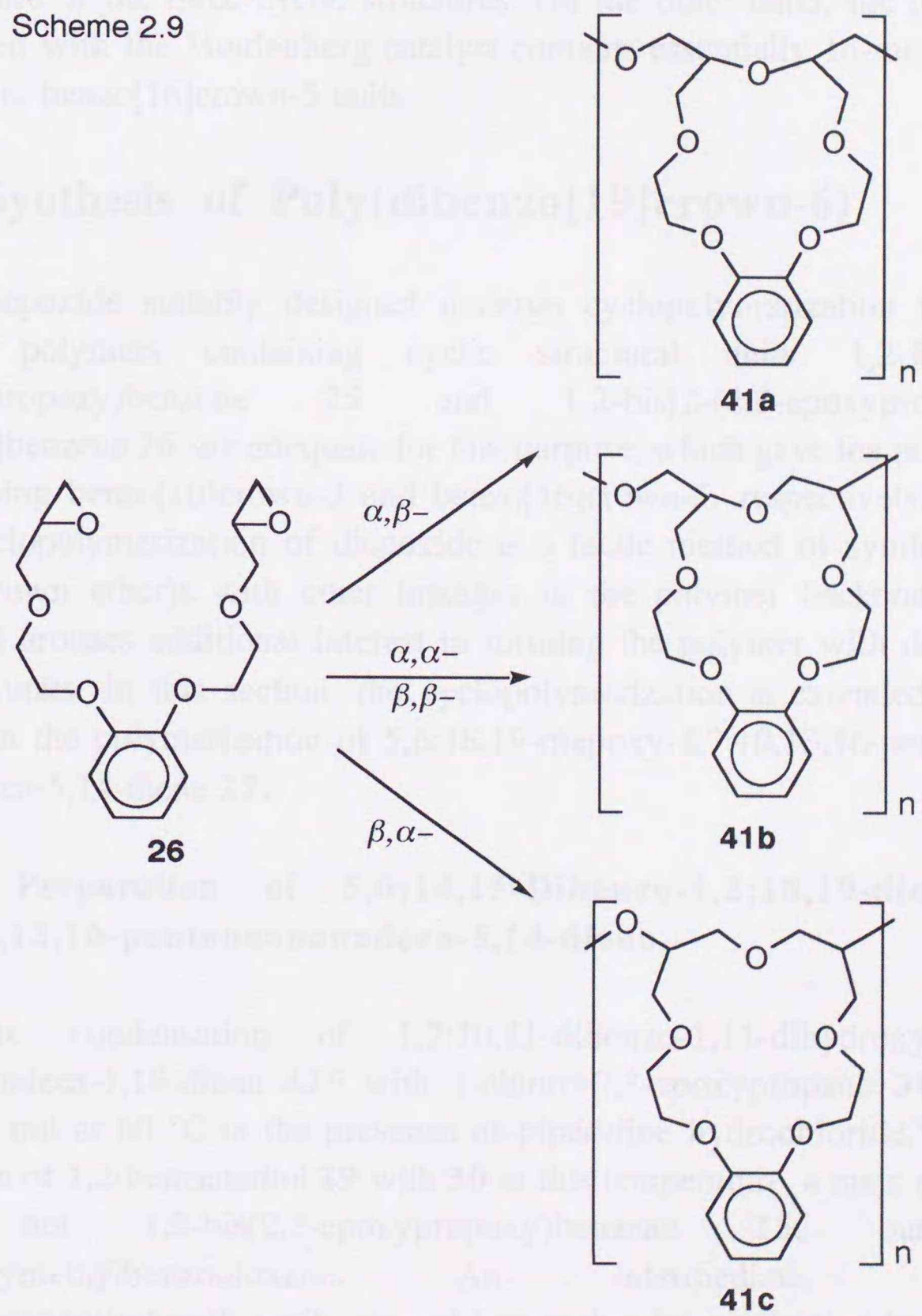


Figure 2.6. ^{13}C NMR spectra of (a) 26 and (b) the polymer prepared by cationic polymerization.

polymerization. The polymer gave the spectra in which the resonances of epoxy group at 44.19 and 50.81 ppm disappeared and three absorptions due to aromatic carbons broadened with somewhat upperfield shift. The latter observation may be dependent upon the conformation of oxyethylene unit in the polymer.

Since all epoxy groups participate in the polymerization forming soluble and gel-free polymers even at high conversions, the resulting products should contain cyclic constitutional units according to the cyclopolymerization mechanism.

Scheme 2.9



2.3.3 Structure of Poly([16]crown-5)

As described in section 2.2.2, the ring opening of **26** in the intramolecular propagation may involve additions due to α,α– or β,β–scissions leading to 16-membered rings (polymer **41b**), whereas α,β– and β,α–scissions should induce intramolecular additions producing 17- and 15-membered rings (polymer **41a** and **c**), respectively (Scheme 2.9). The polymer obtained with ordinary acid catalysts may, therefore, represent a mixture of the three cyclic structures. On the other hand, the polymer prepared with the Vandenberg catalyst contains essentially 16-membered rings i.e. benzo[16]crown-5 units.

2.4 Synthesis of Poly(dibenzo[19]crown-6)

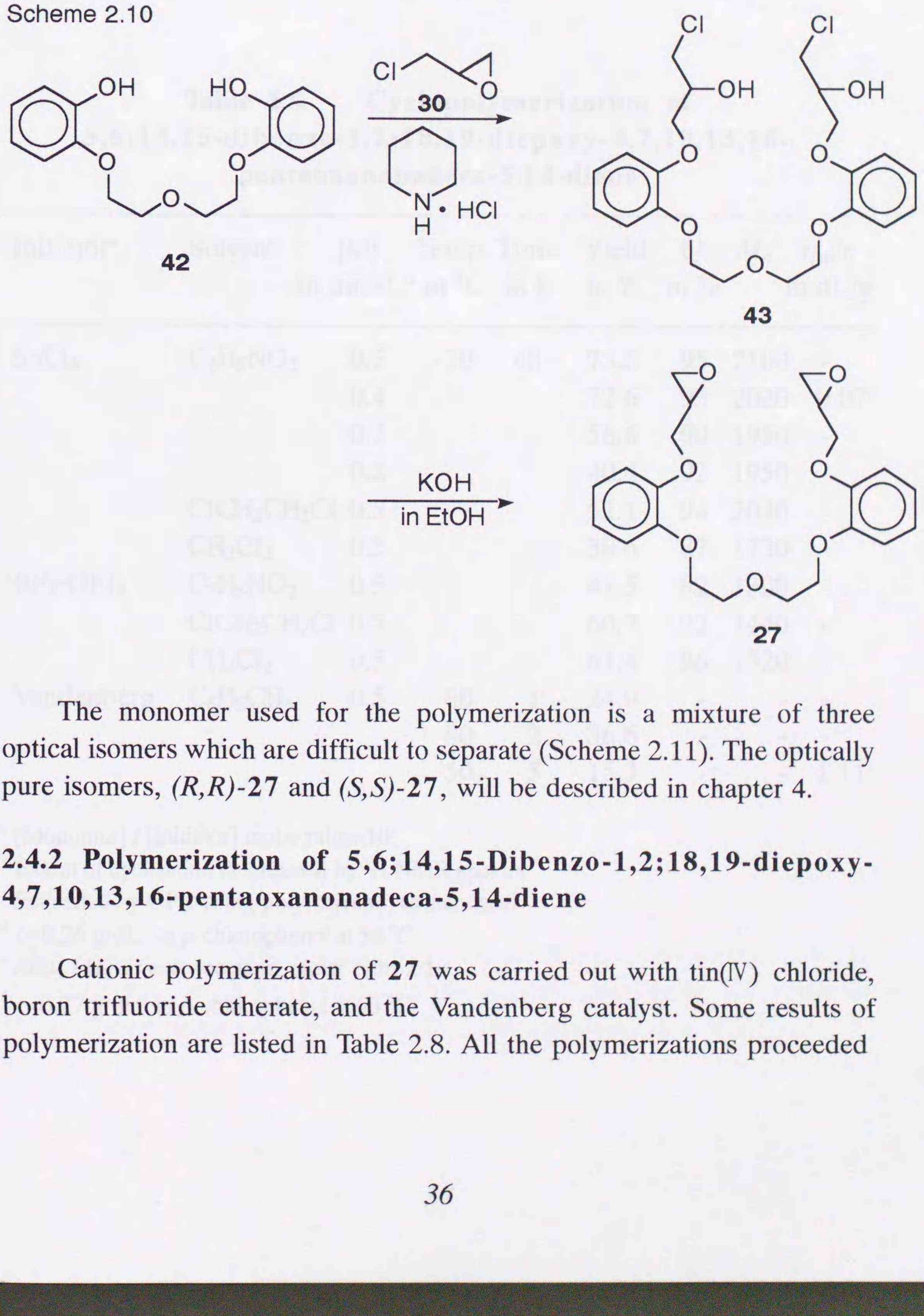
Diepoxide suitably designed undergo cyclopolymerization to give linear polymers containing cyclic structural units. 1,2-Bis(2,3-epoxypropoxy)benzene **25** and 1,2-bis[2-(2,3-epoxypropoxy)-ethoxy]benzene **26** are adequate for this purpose, which gave the polymers containing benzo[10]crown-3 and benzo[16]crown-5, respectively. Thus, the cyclopolymerization of diepoxide is a facile method of synthesizing poly(crown ether)s with ether linkages in the polymer backbone. The method arouses additional interest in forming the polymer with dibenzo-crown units. In this section, the cyclopolymerization is extended to the study in the polymerization of 5,6:18,19-diepoxy-4,7,10,13,16-pentaoxa-nonadeca-5,14-diene **27**.

2.4.1 Preparation of 5,6;14,15-Dibenzo-1,2;18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene

The condensation of 1,2:10,11-dibenzo-1,11-dihydroxy-3,6,9-trioxaundeca-1,10-diene **42**[21] with 1-chloro-2,3-epoxypropane **30** was carried out at 60 °C in the presence of piperidine hydrochloride.[8] In the reaction of 1,2-benzenediol **29** with **30** at this temperature, a main product was not 1,2-bis(2,3-epoxypropoxy)benzene **25**, but 2-hydroxymethylbenzodioxane. An intermediate, 2-(2,3-epoxypropoxy)phenol, easily caused intramolecular cyclization to form a

6-membered ring. In the case of **42**, the undesired side-reaction is eliminated, because the intramolecular cyclization hardly forms a 15-membered ring, and thereby the condensation at this temperature gave a good yield of bischlorohydrin **43**. By treatment in alcoholic potassium hydroxide solution at -10 °C, bischlorohydrin **43** was converted to 5,6:14,15-dibenzo-1,2:18,19-diepoxidy-4,7,10,13,16-pentaoxanonadeca-5,14-diene **27** (Scheme 2.10).

Scheme 2.10

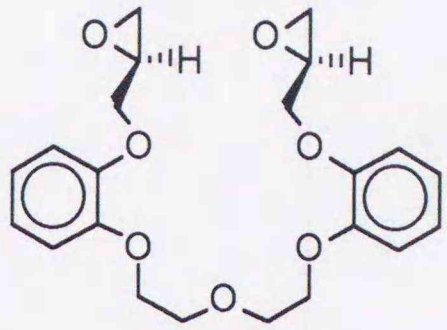


The monomer used for the polymerization is a mixture of three optical isomers which are difficult to separate (Scheme 2.11). The optically pure isomers, *(R,R)*-**27** and *(S,S)*-**27**, will be described in chapter 4.

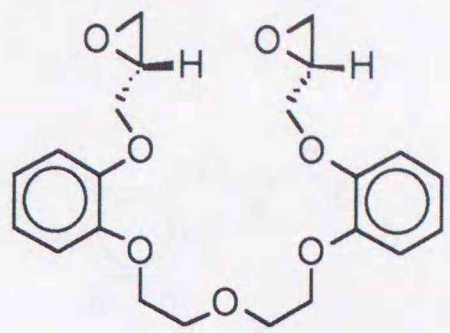
2.4.2 Polymerization of 5,6;14,15-Dibenzo-1,2;18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene

Cationic polymerization of **27** was carried out with tin(Ⅳ) chloride, boron trifluoride etherate, and the Vandenberg catalyst. Some results of polymerization are listed in Table 2.8. All the polymerizations proceeded

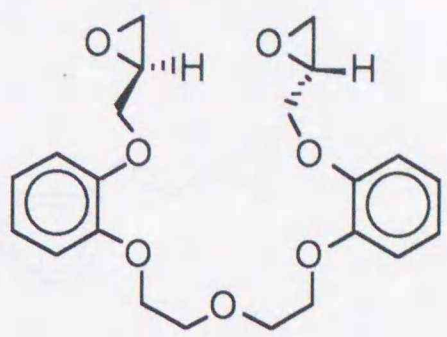
Scheme 2.11



(*S*,*S*)-**27**



(*R*,*R*)-**27**



meso-**27**

Table 2.8. Cyclopolymerization of 5,6;14,15-dibenzo-1,2;18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene

Initiator[a]	Solvent	[M] in mol•L^{-1}	Temp. in °C	Time in h	Yield in %	f_c[b] in %	$\overline{M}_n$[c]	η_{sp}/c in dL/g
$SnCl_4$	$C_2H_5NO_2$	0.5	-30	48	73.5	95	2100	-
		0.4			72.6	93	2020	0.07[d]
		0.3			56.6	90	1950	-
		0.2			40.4	92	1950	-
	$ClCH_2CH_2Cl$	0.5			52.1	94	2040	-
	CH_2Cl_2	0.5			38.6	87	1730	-
$BF_3•OEt_2$	$C_2H_5NO_2$	0.5			41.5	82	1300	-
	$ClCH_2CH_2Cl$	0.5			60.7	92	1440	-
	CH_2Cl_2	0.5			61.4	86	1320	-
Vandenberg[e]	$C_6H_5CH_3$	0.5	80	1	24.9	-	-	-
			80	2	36.6	-	-	-
			50	5	15.3	-	-	1.11[f]

[a] [Monomer] / [Initiator] molar ratio=10.

[b] Extent of cyclization determined by ^{1}H NMR spectra.

[c] Estimated by GPC using poly(styrene) as standard.

[d] c=0.26 g•dL^{-1} in *p*-chlorophenol at 50 °C.

[e] $AlEt_3$ / H_2O / acetylacetone, molar ratio 2:1:1.

[f] c=0.27 g•dL^{-1} in *p*-chlorophenol at 50 °C.

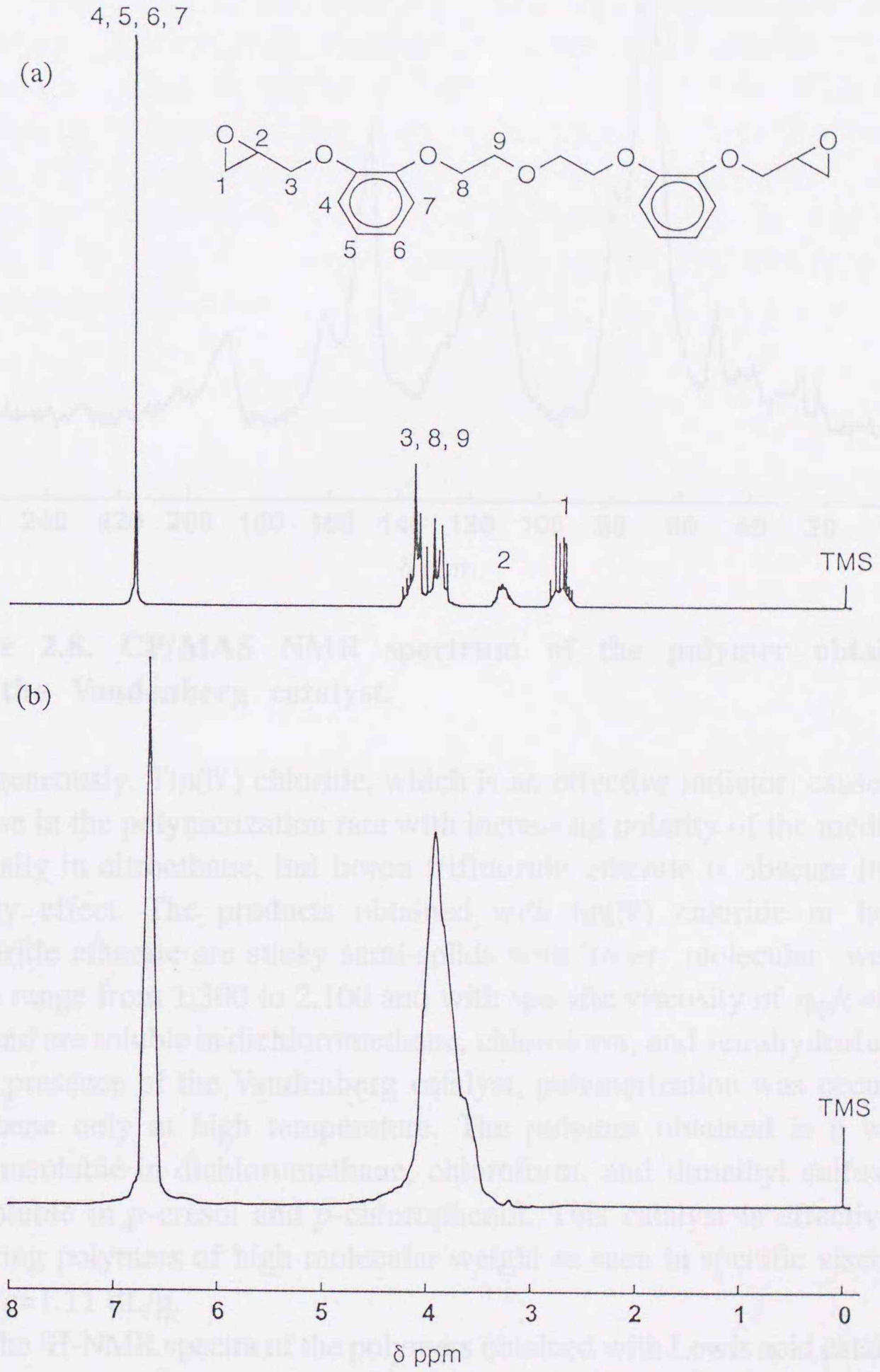


Figure 2.7. ^{1}H NMR spectra of (a) 5,6;14,15-dibenzo-1,2;18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene (27) and (b) its polymer obtained with Lewis acid catalyst.

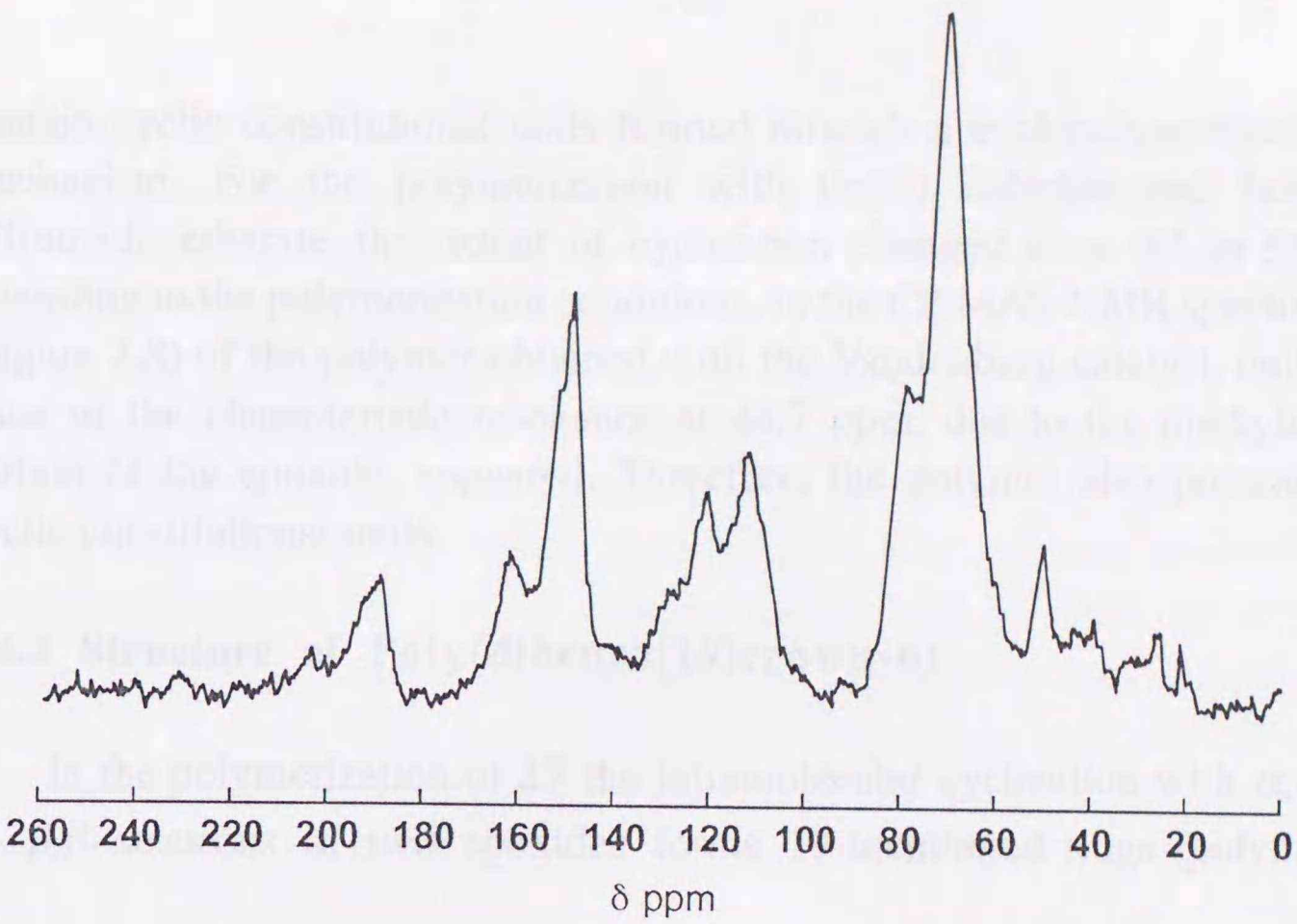


Figure 2.8. CP/MAS NMR spectrum of the polymer obtained with the Vandenberg catalyst.

homogeneously. Tin(Ⅳ) chloride, which is an effective initiator, causes an increase in the polymerization rate with increasing polarity of the medium, especially in nitroethane, but boron trifluoride etherate is obscure in the polarity effect. The products obtained with tin(Ⅳ) chloride or boron trifluoride etherate are sticky semi-solids with lower molecular weight in the range from 1,300 to 2,100 and with specific viscosity of η_{sp}/c=0.07 dL/g and are soluble in dichloromethane, chloroform, and tetrahydrofuran. In the presence of the Vandenberg catalyst, polymerization was occurred in toluene only at high temperature. The polymer obtained is a white solid, insoluble in dichloromethane, chloroform, and dimethyl sulfoxide, and soluble in *p*-cresol and *p*-chlorophenol. This catalyst is effective in preparing polymers of high molecular weight as seen in specific viscosity of η_{sp}/c=1.11 dL/g.

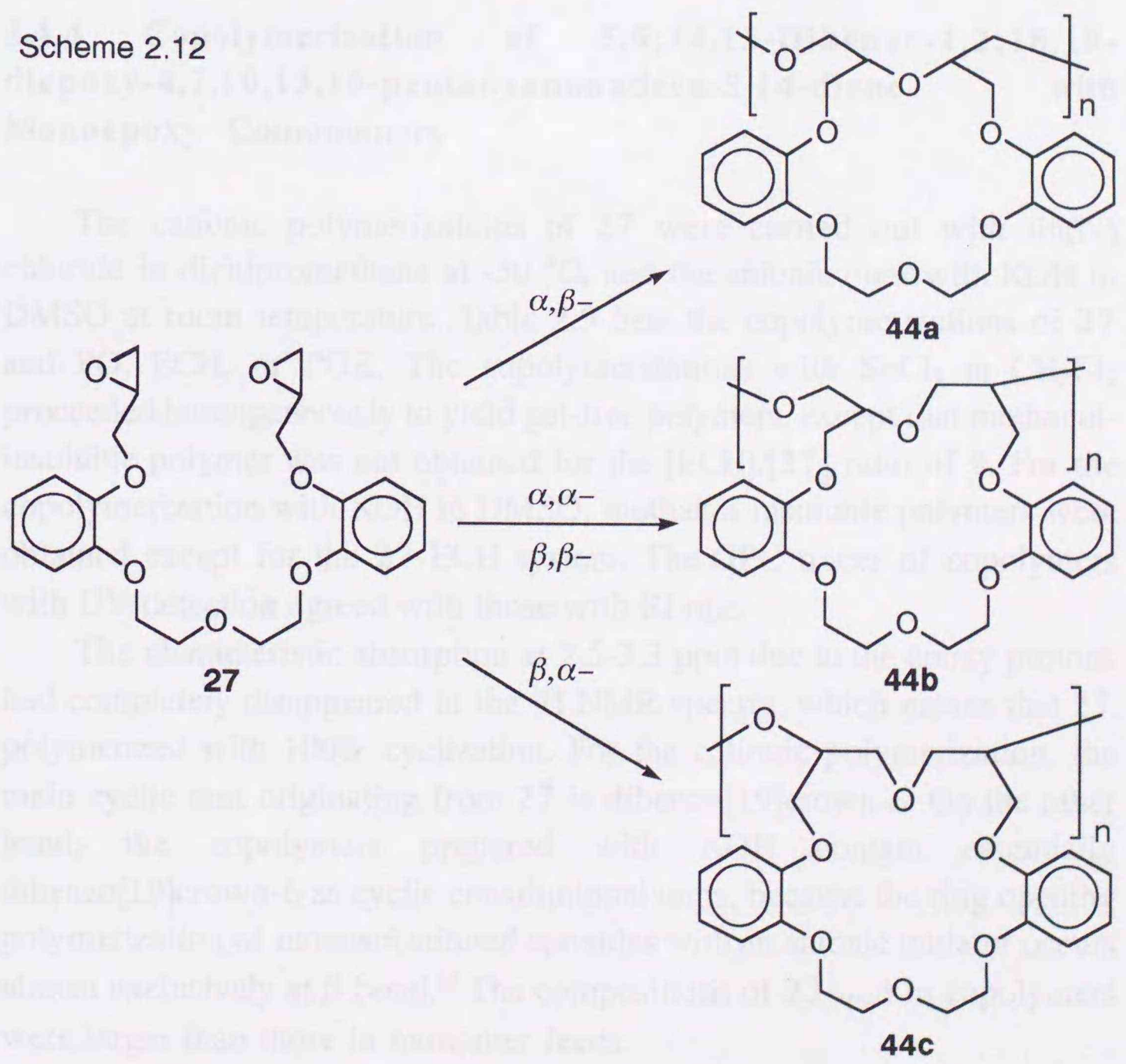
The ^{1}H-NMR spectra of the polymers obtained with Lewis acid catalysts showed that the characteristic resonances at δ=2.7 and 3.3 ppm, due to the methylene and the methine protons of the epoxide, can be slightly detected (Figure 2.7). Since most of the epoxy groups participated in the polymerization forming soluble and gel-free polymers, the polymers should

contain cyclic constitutional units formed through a cyclopolymerization mechanism. For the polymerization with tin(IV) chloride and boron trifluoride etherate, the extent of cyclization changed from 82 to 95% according to the polymerization conditions. In the CP/MAS-NMR spectrum (Figure 2.8) of the polymer obtained with the Vandenberg catalyst, only a trace of the characteristic resonance at 44.7 ppm, due to the methylene carbon of the epoxide, appeared. Therefore, the polymer also possesses cyclic constitutional units.

2.4.3 Structure of Poly(dibenzo[19]crown-6)

In the polymerization of **27** the intramolecular cyclization with α,α– or β,β–scissions of two epoxides forms 19-membered rings (polymer

Scheme 2.12



44b), whereas α,β– and β,α–scissions lead to the formation of 18- and 20-membered rings (polymer **44a** and **c**), respectively (Scheme 2.12).

Because many epoxides have shown to subject to both α– and β–scissions under acidic conditions, the polymer **44** obtained with ordinary acid catalyst may represent a mixture of three possible cyclic units. The random orientation of ring opening, however, gives 50% of dibenzo[19]crown units, polymer **44b**, as main constitutional units. In the polymerization of propylene oxide with the coordinating catalyst, ring opening of epoxide has been found to be occurred predominantly in β-position, therefore, suggesting that the polymer prepared with the Vandenberg catalyst contains essentially dibenzo[19]crown-6 units. It appears well established that the polymerization of **27** gives the cyclic polymer mainly consisting of dibenzo[19]crown-6 units, namely poly(dibenzo[19]crown-6).

2.4.4 Copolymerization of 5,6;14,15-Dibenzo-1,2;18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene with Monoepoxy Comonomers

The cationic polymerizations of **27** were carried out with tin(Ⅳ) chloride in dichloromethane at -30 °C, and the anionic ones with KOH in DMSO at room temperature. Table 2.9 lists the copolymerizations of **27** and PO, ECH, or PGE. The copolymerizations with $SnCl_4$ in CH_2Cl_2 proceeded homogeneously to yield gel-free polymers, except that methanol-insoluble polymer was not obtained for the [ECH]/[**27**] ratio of 9. For the copolymerization with KOH in DMSO, methanol-insoluble polymers were obtained except for the **27**-ECH system. The GPC traces of copolymers with UV detection agreed with those with RI one.

The characteristic absorption at 2.5-3.3 ppm due to the epoxy protons had completely disappeared in the ^{1}H NMR spectra, which means that **27** polymerized with 100% cyclization. For the cationic polymerization, the main cyclic unit originating from **27** is dibenzo[19]crown-6. On the other hand, the copolymers prepared with KOH contain essentially dibenzo[19]crown-6 as cyclic constitutional units, because the ring opening polymerization of monosubstituted epoxides with an anionic initiator occurs almost exclusively at β-bond.[17] The compositions of **27** unit in copolymers were larger than those in monomer feeds.

Table 2.9. Copolymerizations of 5,6:14,15-dibenzo-1,2:18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene (27) with propylene oxide (PO), epichlorohydrin (ECH), and phenyl glycidyl ether (PGE)[a]

Epoxy monomer (EM)	Initiator (I)	Mole Fraction of **27**	[**27**+EM] mol•L^{-1} in feed	[I] mol•L^{-1}	Time h	Yield %	Mole Fraction of **27** in copolymer[b]	$\overline{M}_n$ x10^{-3} [c]
PO	$SnCl_4$	0.50[d]	0.5	0.05	9	4	0.73	2.0
	$SnCl_4$	0.30[d]	1.0	0.1	20	12	0.56	1.9
	KOH	0.50[e]	0.5	0.05	8	15	0.90	1.2
ECH	$SnCl_4$	0.50[d]	0.5	0.05	9	20	0.89	2.3
	$SnCl_4$	0.10[d]	2.0	0.2	25	0	-	-
	KOH	0.50[e]	0.5	0.05	168	0	-	-
PGE	$SnCl_4$	0.50[d]	0.5	0.05	9	22	0.89	2.1
	$SnCl_4$	0.10[d]	2.0	0.2	25	6	0.58	2.1
	KOH	0.50[e]	0.5	0.05	5	36	0.81	3.1

[a] Temp, -30 °C for $SnCl_4$ in CH_2Cl_2; 23 °C for KOH in DMSO.
[b] Determined by ^{1}H NMR spectra.
[c] Determined by GPC (polystyrene calibration).
[d] Solvent, CH_2Cl_2.
[e] Solvent, DMSO.

2.5 Synthesis of Poly(hemispherand)

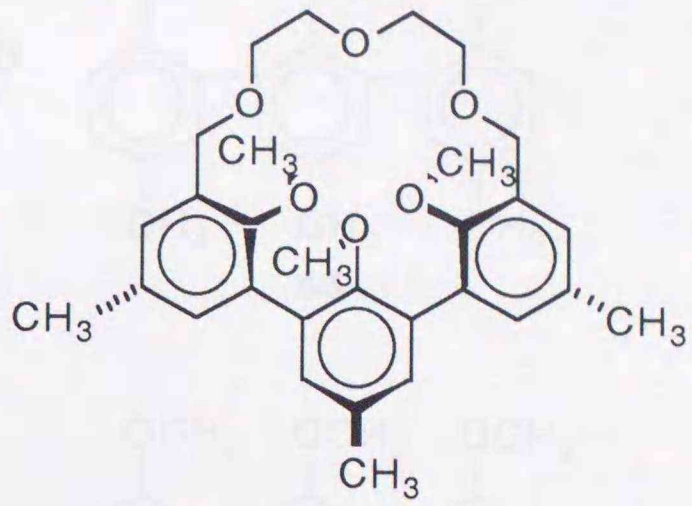
Since the discovery of dibenzo[18]crown-6,[22] many kinds of macrocyclic systems have been designed and synthesized as hosts in host-guest chemistry.[23] Hemispherand[24] **45** and spherand **46** (Scheme 2.13), which are based on 2,6-disubstituted 4-methyl anisole units, are classified as a group of host compounds. They are organized prior to complexation and form a capsular complex with a cationic guest.[25] In polymer chemistry, various polymers with crown ether or other macrocyclic units are synthesized and their host abilities are examined in the appropriate host-guest

systems.[26] However, there has been no attempt to prepare polymers with **45** or **46** unit. This section reports on the synthesis and the cyclopolymerization of diepoxide, 2,6- bis [3 - (4,5 - epoxy -2- oxa-pentyl) - 2 - methoxy -5- methyl-phenyl]-4-methylanisole **28**, and the cation binding property of the resulting poly(hemispherand).

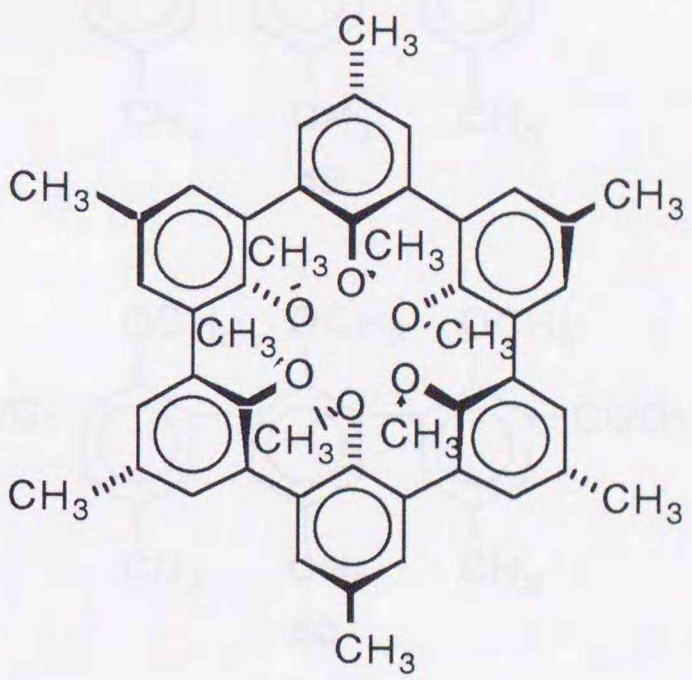
2.5.1 Preparation of 2,6-Bis [3-(4,5-epoxy-2-oxapentyl)-2-methoxy-5-methylphenyl]-4-methylanisole

Oxidation of *p*-cresole **47** with ferric chloride hexahydrate ($FeCl_3 \cdot 6H_2O$) gave triphenol **48**. Three hydroxy groups in **48** were methylated with dimethyl sulfate to provide trianisole **49**. Lithiation and followed by carboxylation of **49** led to the production of diacid **50** which was further reduced with boron trifluoride-tetrahydrofuran complex ($BF_3 \cdot THF$) to give diol **51**. A phase-transfer reaction with tetrabutylammonium hydrogen sulfate as a catalyst was very useful for the condensation of **51** with **30**, thereby producing **28** (Scheme 2.14).

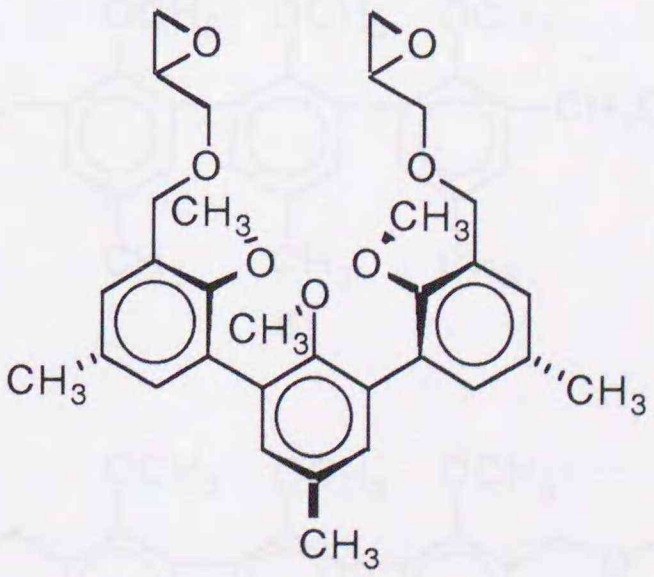
Scheme 2.13



45

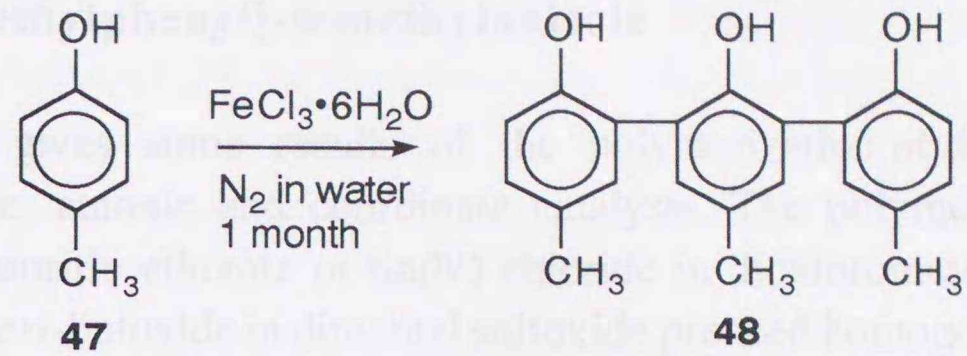


46

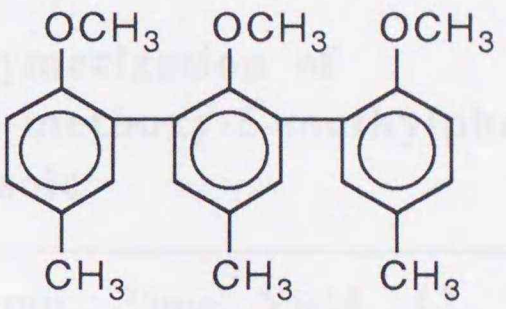


28

Scheme 2.14



47 48



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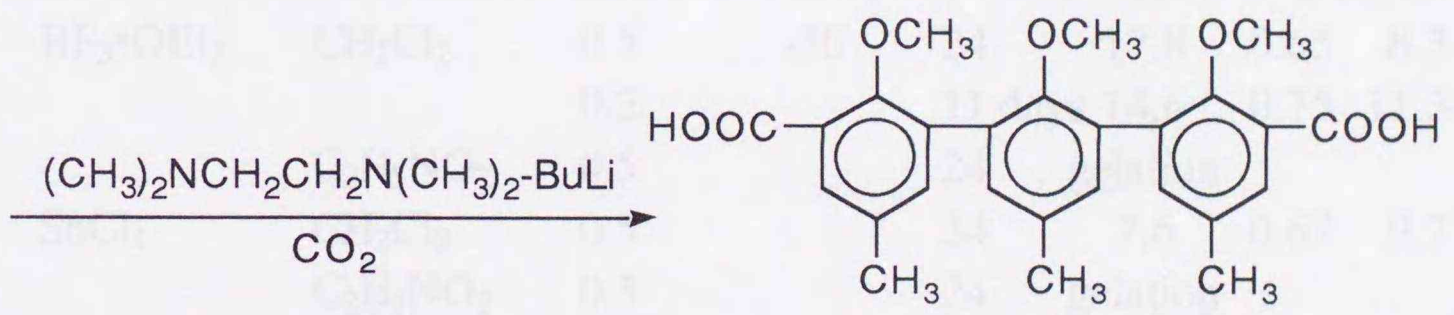

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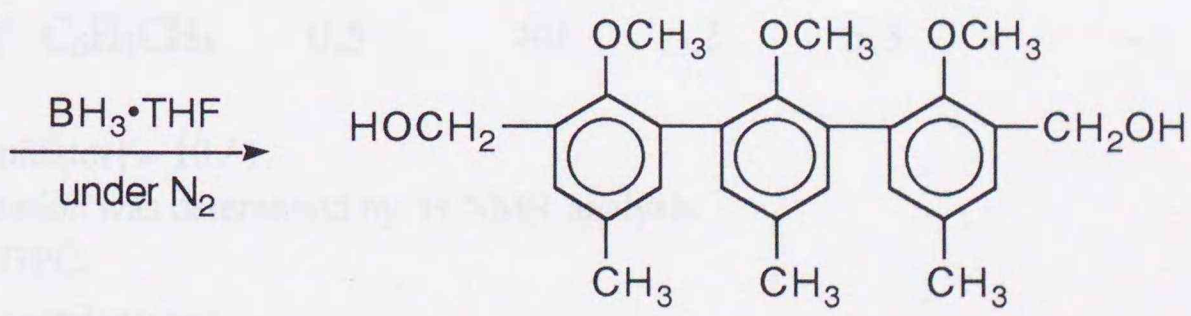
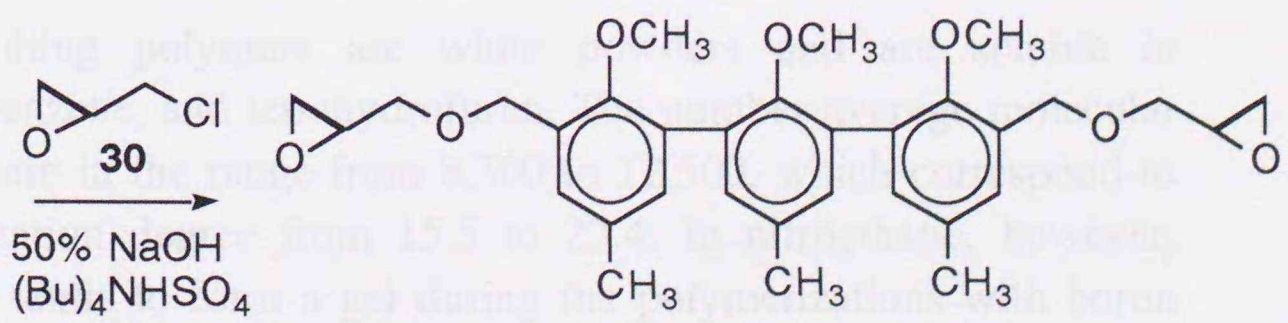


51



28

2.5.2 Polymerization of 2,6-Bis[3-(4,5-epoxy-2-oxapentyl)-2-methoxy-5-methylphenyl]-4-methylanisole

Table 2.10 gives some results of the polymerization of diepoxide **28** with cationic, anionic and coordinate catalysts. The polymerizations with boron trifluoride etherate or tin(IV) chloride in dichloromethane and with potassium *tert*-butoxide in dimethyl sulfoxide proceed homogeneously.

Table 2.10. Cyclopolymerization of 2,6-bis[3-(4,5-epoxy-2-oxapentyl)-2-methoxy-5-methylphenyl]-4-methylanisole[a]

Initiator (I)	Solvent	[Monomer] in mol•L^{-1}	Temp. in °C	Time in h	Yield in %	f_c[b]	$\overline{M}_n$[c] x10^{-3}
BF_3•OEt_2	CH_2Cl_2	0.5	-30	24	17.8	0.65	8.3
		0.2		11 days	14.6	0.75	11.3
	$C_2H_5NO_2$	0.5		24	gelation		
$SnCl_4$	CH_2Cl_2	0.5		24	7.6	0.67	9.7
	$C_2H_5NO_2$	0.5		24	gelation		
t-BuOK	DMSO	0.5	r.t.	7	7.8	0.65	12.5
KOH	DMSO	0.5	r.t.	7 days	0	-	-
Vandenberg[d]	$C_6H_5CH_3$	0.5	80	2	5.3	-	-

[a] [Monomer] / [Initiator] = 10 / 1.

[b] Extent of cyclization was determined by ^{1}H NMR analysis.

[c] Determined by GPC.

[d] $2AlEt_3$ / H_2O / acetylacetone.

The resulting polymers are white powders and are soluble in chloroform, benzene, and tetrahydrofuran. The number average molecular weights ($\overline{M}_n$) are in the range from 8,300 to 12,500, which correspond to the polymerization degree from 15.5 to 23.4. In nitroethane, however, monomer **28** tends to form a gel during the polymerizations with boron

trifluoride etherate or tin(Ⅳ) chloride. Potassium hydroxide, which was the effective initiator for the polymerization of diepoxide **27**, does not perform the initiation of **28**. In the presence of the Vandenberg catalyst, the polymerization system is homogeneous, but the polymer obtained is insoluble in chloroform, tetrahydrofuran, *p*-chlorophenol, and other common organic solvents. The polymer from **27** with this catalyst had a

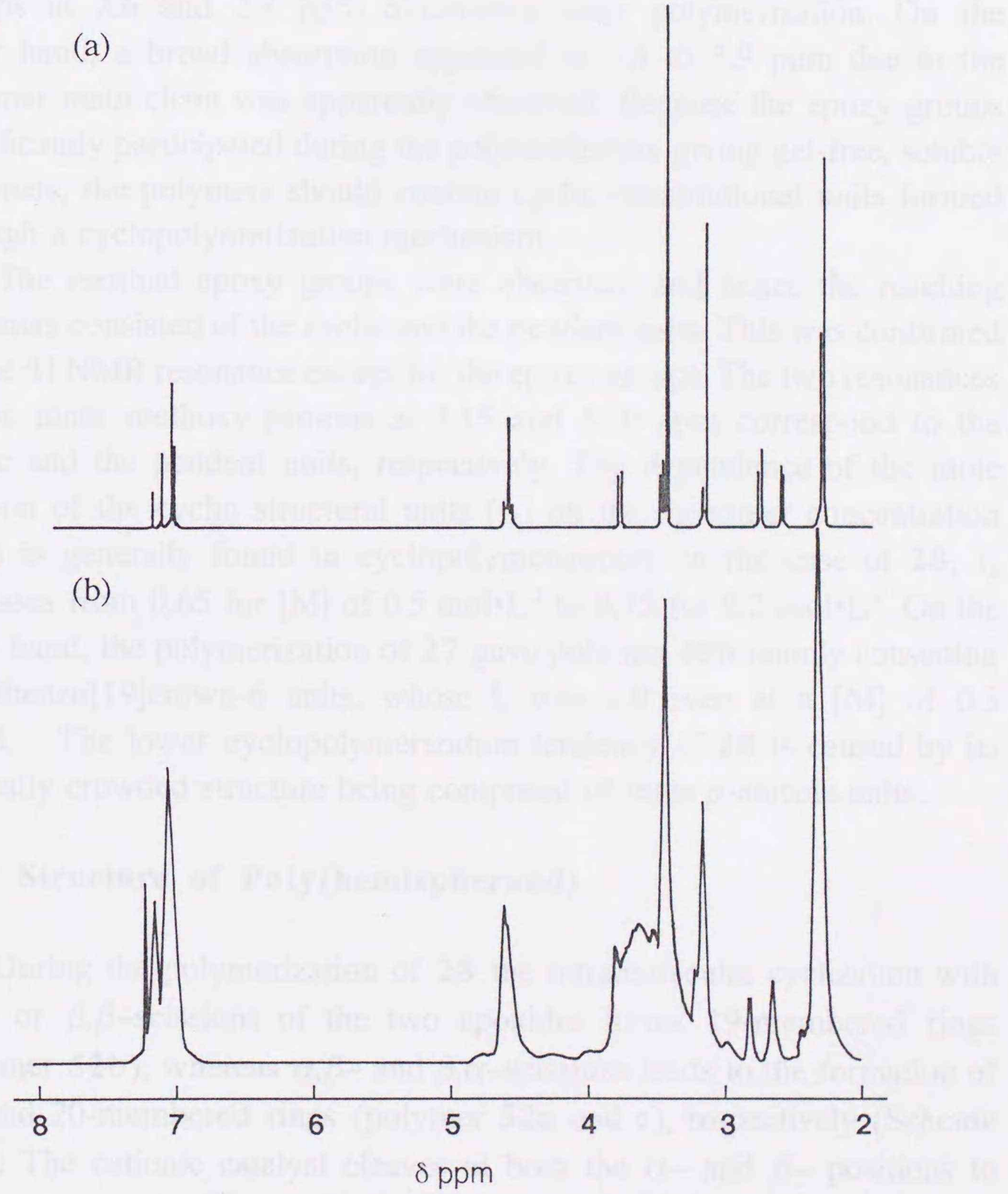


Figure 2.9. ^{1}H NMR spectra of (a) 28 and (b) its polymer obtained with *t*-BuOK in DMSO.

significantly higher viscosity than that with cationic ones. With regard to **28**, the insolubility is accordingly caused not by the presence of a three-dimensional network structure in the polymer, but by its higher molecular weight.

Figure 2.9 shows the ^{1}H NMR spectra of monomer **28** and its polymer obtained with potassium *tert*-butoxide. In the spectrum of the polymer, the characteristic resonance due to the methylene protons of the epoxy groups at 2.6 and 2.8 ppm diminished after polymerization. On the other hand, a broad absorption appeared at 3.3 to 3.9 ppm due to the polymer main chain was apparently observed. Because the epoxy groups significantly participated during the polymerization giving gel-free, soluble polymers, the polymers should contain cyclic constitutional units formed through a cyclopolymerization mechanism.

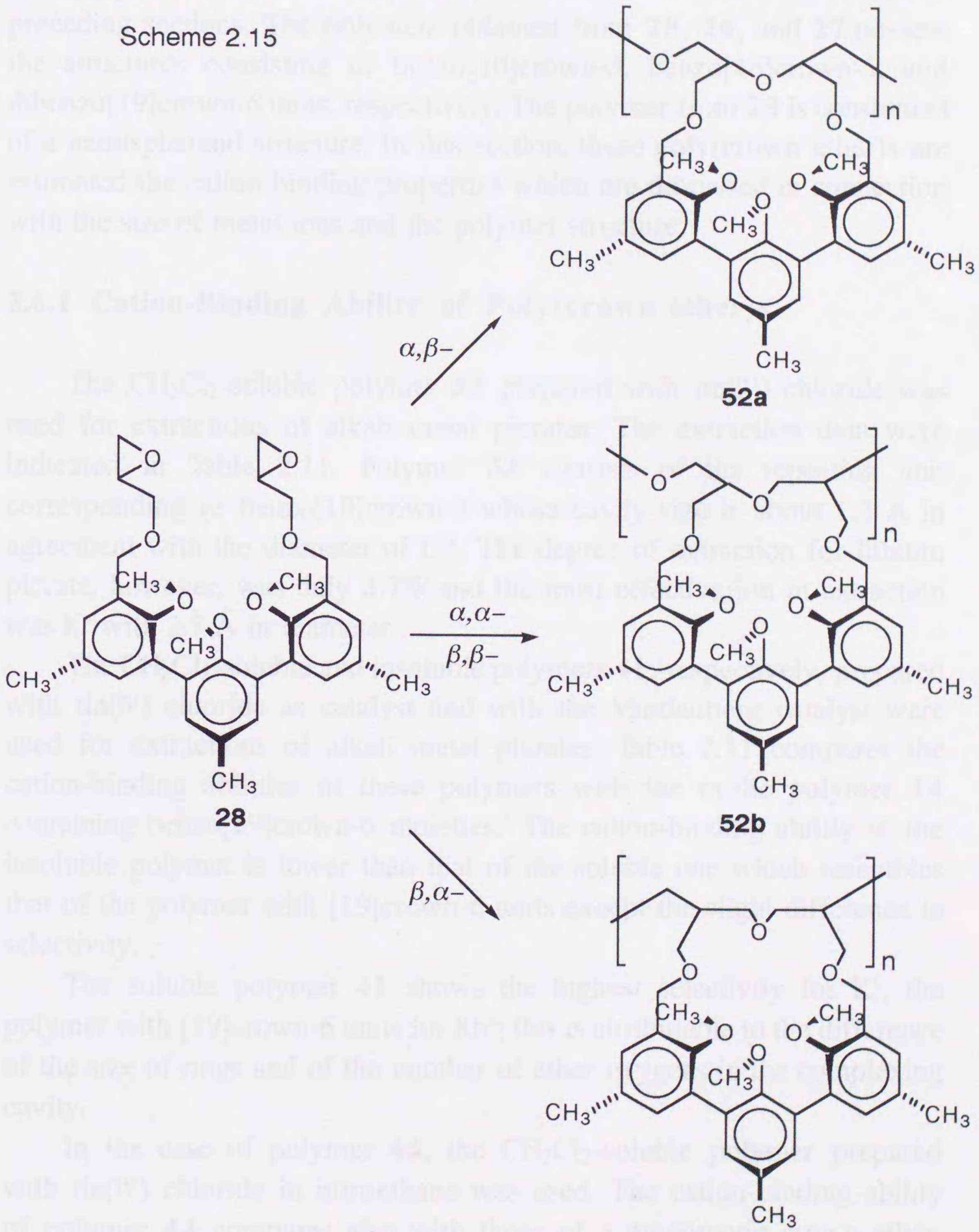
The residual epoxy groups were observed, and hence the resulting polymers consisted of the cyclic and the pendant units. This was confirmed by the ^{1}H NMR resonance except for the epoxy groups. The two resonances of the inner methoxy protons at 3.15 and 3.20 ppm correspond to the cyclic and the pendent units, respectively. The dependence of the mole fraction of the cyclic structural units (f_c) on the monomer concentration ([M]) is generally found in cyclopolymerization. In the case of **28**, f_c increases from 0.65 for [M] of 0.5 mol•L^{-1} to 0.75 for 0.2 mol•L^{-1}. On the other hand, the polymerization of **27** gave polymer **45b** mainly consisting of dibenzo[19]crown-6 units, whose f_c was 1.0 even at a [M] of 0.5 mol•L^{-1}. The lower cyclopolymerization tendency of **28** is caused by its sterically crowded structure being composed of three *p*-anisole units.

2.5.3 Structure of Poly(hemispherand)

During the polymerization of **28** the intramolecular cyclization with α,α– or β,β–scissions of the two epoxides forms 19-membered rings (polymer **52b**), whereas α,β– and β,α–scissions leads to the formation of 18- and 20-membered rings (polymer **52a** and **c**), respectively (Scheme 2.15). The cationic catalyst cleaves at both the α– and β– positions to yield polymers having a mixture of three possible cyclic units, polymers **52a**, **b**, and **c**. The random orientation of ring-opening forms the main constitutional units with at least 50% of the 19-membered hemispherand,

polymer **52b**, as the main cyclic units. On the other hand, an anionic catalyst cleaves the β– bond. The polymer prepared with potassium *tert*-butoxide, therefore, contains the 19-membered hemispherand polymer **52b** as the cyclic constitutional units.

Scheme 2.15



2.6 Cation-Binding Ability

Diepoxides **25**, **26**, **27**, and **28** were polymerized through the cyclopolymerization mechanism under the conditions described in the preceding sections. The polymers obtained from **25**, **26**, and **27** possess the structures consisting of benzo[10]crown-3, benzo[16]crown-5, and dibenzo[19]crown-6 units, respectively. The polymer from **28** is constituted of a hemispherand structure. In this section, these poly(crown ether)s are estimated the cation-binding properties which are discussed in connection with the size of metal ions and the polymer structure.

2.6.1 Cation-Binding Ability of Poly(crown ether)s

The CH_2Cl_2-soluble polymer **33** prepared with tin(Ⅳ) chloride was used for extractions of alkali metal picrates. The extraction data were indicated in Table 2.11. Polymer **33** consists of the repeating unit corresponding to benzo[10]crown-3 whose cavity size is about 1.2 Å in agreement with the diameter of Li^+. The degree of extraction for lithium picrate, however, was only 3.7% and the most effective ion in extraction was K^+ with 2.7 Å in diameter.

The CH_2Cl_2-soluble and insoluble polymers **41**, respectively, prepared with tin(Ⅳ) chloride as catalyst and with the Vandenberg catalyst were used for extractions of alkali metal picrates. Table 2.11 compares the cation-binding abilities of these polymers with the cyclic polymer **14** containing benzo[19]crown-6 moieties.[2] The cation-binding ability of the insoluble polymer is lower than that of the soluble one which resembles that of the polymer with [19]crown-6 units except the slight difference in selectivity.

The soluble polymer **41** shows the highest selectivity for K^+, the polymer with [19]crown-6 units for Rb^+; this is attributable to the difference of the size of rings and of the number of ether oxygens in the complexing cavity.

In the case of polymer **44**, the CH_2Cl_2-soluble polymer prepared with tin(Ⅳ) chloride in nitroethane was used. The cation-binding ability of polymer **44** compares also with those of a monomeric crown ether, dibenzo[18]crown-6 **6**, in Table 2.11. The ability of the polymer is slightly

less effective and selective in binding cation than that of the model compound. Polymers **41** and **44** showed the highest selectivity for K^+, but poly(benzo[19]crown-6] showed that for Rb^+.

Extraction yield of poly[([10]crown-3)$_{0.43}$-*co*-PGE$_{0.57}$] was shown in Table 2.11. The incorporation of the spaces (poly(PEG) units) into poly(**33**-*co*-**38**) decreased the extraction of alkali-metal cations. The crown structure from **25** corresponded to benzo[10]crown-3 whose ring size is smaller than that of alkali-metal cations. Therefore, the crown structure of polymer **33** unit complexed with cations by neighboring crown ring owing to cooperative effect.

Table 2.11. Extraction of alkali picrates into the methylene chloride phase[a]

Complexing agent	Extraction yield in % of picrates				
	Li^+	Na^+	K^+	Rb^+	Cs^+
Polymer **33**[b]	3.7	20.9	33.5	23.9	16.5
Polymer **41**[b]	12.7	41.2	78.5	75.6	61.5
Polymer **41**[c]	5.4	16.2	38.6	38.9	30.1
Polymer **44**[b]	6.3	31.4	82.2	77.4	67.5
Polymer **33**-*co*-**PGE**[d]	0.0	13.9	25.7	16.9	10.7
Poly([19]crown-6)[e]	4.7	38.0	78.6	80.8	79.0
Dibenzo[18]crown-6[f]	3.7	18.3	93.5	84.9	81.6

[a] [Picric acid]=7x10-5 mol•L^{-1}; [Crown units]=3.5x10-3 mol•L^{-1}; [Metal hydroxide]=0.1 mol•L^{-1}.

[b] CH_2Cl_2-soluble polymer prepared with $SnCl_4$.

[c] CH_2Cl_2-insoluble polymer prepared with Vandenberg catalyst. The specimen swelled in methylene chloride (23.2 times of its original weight).

[d] Poly[([10]crown-3)$_{0.43}$-*co*-PGE$_{0.57}$].

[e] Ref. 2.

[f] Ref. 29.

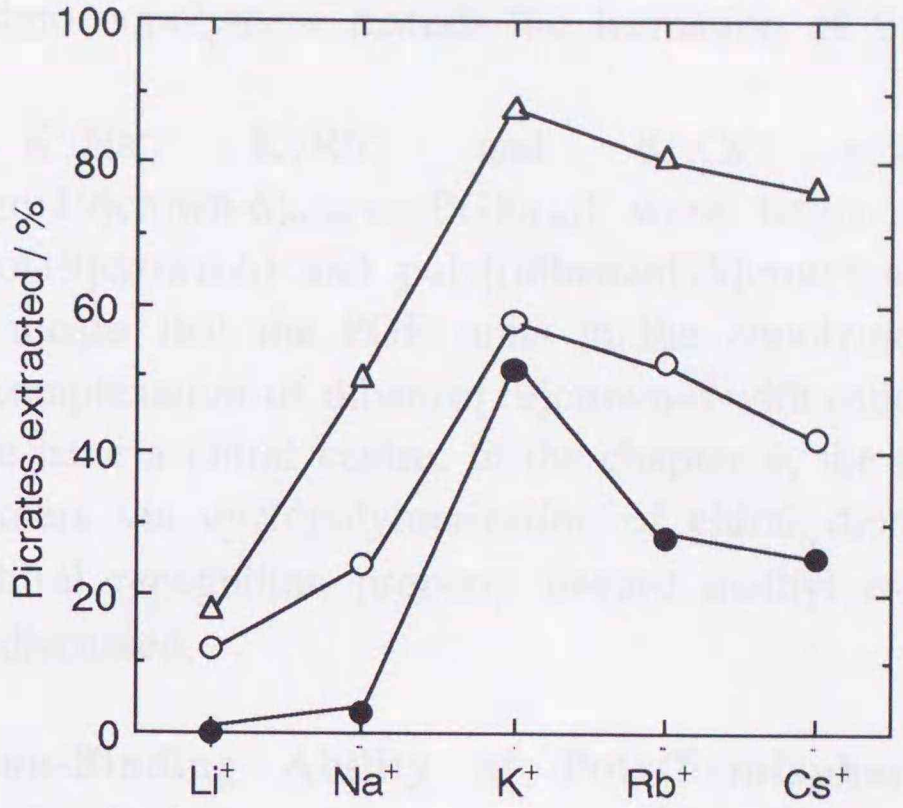


Figure 2.10. Extraction yield (%) of alkali-metal picrates by poly[(dibenzo[19]crown-6)$_{0.56}$-*co*-PO$_{0.44}$] (○), poly[(dibenzo[19]crown-6)$_{0.58}$-*co*-PGE$_{0.42}$] (●), and poly(dibenzo[19]crown-6) (△): [crown ether units in polymer]=3.5x10^{-3} mol•L^{-1} in CH_2Cl_2 phase; [picric acid]=7x10^{-5} mol•L^{-1} and [metal hydroxide] =0.1 mol•L^{-1} in H_2O phase.

Figure 2.10 shows the results of the extraction yields of alkali-metal picrates by poly[(dibenzo[19]crown-6)$_{0.56}$-*co*-PO$_{0.44}$], poly[(dibenzo[19]crown-6)$_{0.58}$-*co*-PGE$_{0.42}$], and poly(dibenzo[19]crown-6) prepared by the cationic cyclopolymerization of **27**. The extraction yields of alkali-metal picrates were increased in order of $K^+ > Rb^+ > Cs^+ >> Na^+ > Li^+$ for each host polymer. Dibenzo[18]crown-6 shows the highest selectivity for K^+, because the diameter of the crown cavity corresponds to that of K^+. On the other hand, the host polymers are considerably more efficient than dibenzo[18]crown-6 in binding K^+, Rb^+, and Cs^+ which have diameters larger than the crown cavity. This result can be explained by cooperative coordination effects, where two neighboring crown ether

rings combine with a single cation. The extraction yields for the copolymers were lower than those for the homopolymer, since the comonomer units introduced into copolymers disturb the formation of 2:1 crown-cation complex.

The K^+/Na^+, K^+/Rb^+, and K^+/Cs^+ selectivities for poly[(dibenzo[19]crown-6)$_{0.58}$-*co*-PGE$_{0.42}$] were larger than those for poly(dibenzo[19]crown-6) and poly[(dibenzo[19]crown-6)$_{0.56}$-*co*-PO$_{0.44}$]. This result means that the PGE units in the copolymer act as steric barrier for complexation of dibenzo[19]crown-6 with cations.

Epoxide have a chiral centre. In the chapter 4, the syntheses chiral crown polymers via cyclopolymerization of chiral diepoxy monomers and their chiral recognition property toward methyl ester of α-amino acid will be discussed.

2.6.2 Cation-Binding Ability of Poly(hemispherand) and its Structural Analysis

The CH_2Cl_2-soluble polymer **52** obtained with boron trifluoride etherate in CH_2Cl_2 (f_c=0.65) was used for the experiment of extraction of alkali metal picrates. The cation-binding property of polymer **52** compares with hemispherand **45**[24] which corresponds closely to the cyclic units in polymer **52**, and with those of dibenzo[18]crown-6 **6** and poly(dibenzo[19]crown-6) **14**, in Figure 2.11. The selectivity which is estimated by the extraction equilibrium constant (K_{ex})[27] is in the order of $Rb^+ > K^+ > Cs^+ > Na^+ > Li^+$ for polymer **52**, $Na^+ > K^+ > Rb^+ > Cs^+ > Li^+$ for **45**, and $K^+ > Rb^+ > Cs^+ > Na^+ > Li^+$ for **6** and **14**. Polymer **14** is slightly less selective and effective in binding for cation than **6**, whereas polymer **52** is noticeably less than **45**. These results indicate that the hemispherand units in polymer **52** do not act as the preorganized spherical cavity like **45**. The chemical shifts of the outer methoxy protons for **45**, monomer **28**, and polymer **52** were almost same, showing in Table 2.12. On the other hand, the upfield shifts of the inner from the outer methoxy protons for **45** are larger than those for monomer **28** and polymer **52**. The larger upfield shift for **45**, which is found in the other hemispherands, reflects that the three methoxy oxygens possess the down-up-down arrangement, which preorganizes the spherical cavity for **45**.[24,28] On the

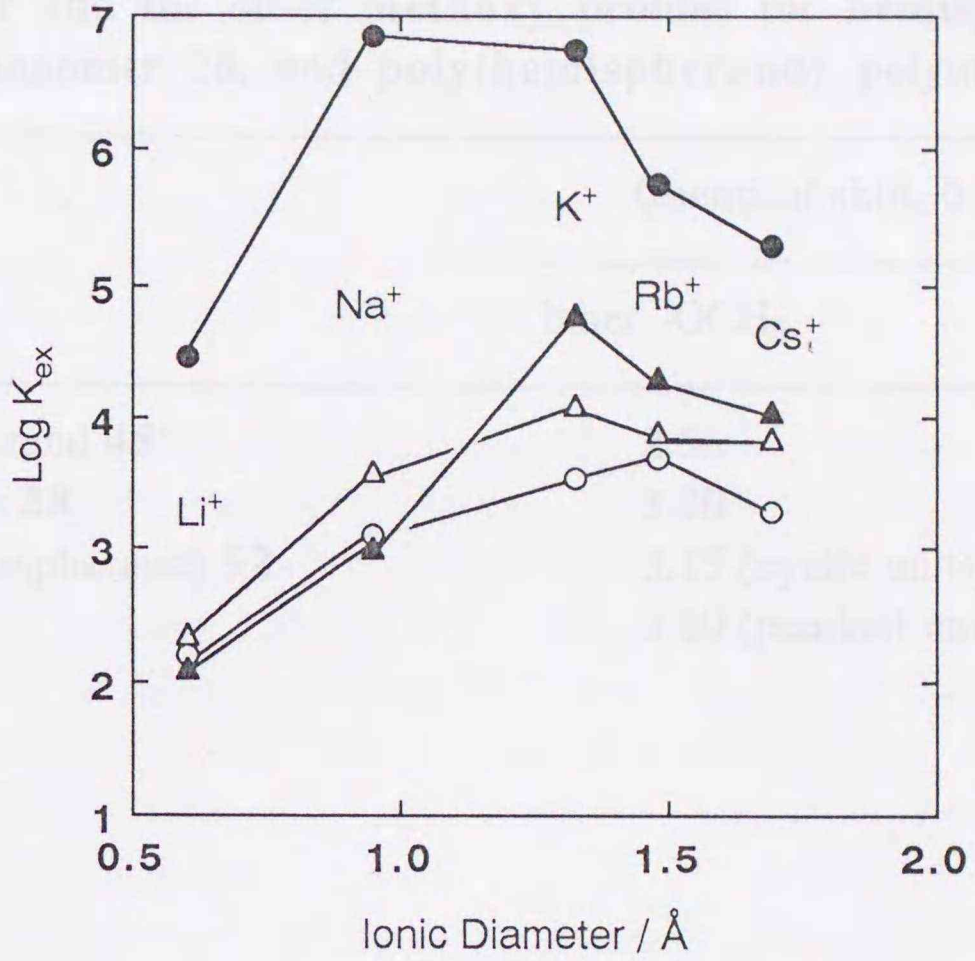


Figure 2.11 Logarithmic plots of extraction equilibrium constant (K_{ex}) of hemispherand (45) (●), poly(hemispherand) (polymer 52) (○), poly(dibenzo[19]crown-6) (polymer 44) (△), and dibenzo[18]crown-6 (6) (▲) toward alkali metal cations: [picric acid] = 3.5×10^{-5} mol•L^{-1}, [metal hydroxide] = 0.1 mol•L^{-1}, [45] = 3.5×10^{-5} mol•L^{-1}, [polymer 52] = 7×10^{-3} mol•L^{-1}, [polymer 44] = [6] = 3.5×10^{-4} mol•L^{-1}.

other hand, the smaller upfield shift for the cyclic units in polymer **52** as well as the acyclic compound, monomer **28**, indicates that the arrangement of the three methoxy oxygens in the cyclic units for polymer **52** is not suitable for the formation of the spherical cavity as in **45**.

These results suggest that the enforced structure of the cavity is different between poly(hemispherand) **52** prepared via the cyclopolymerization method and hemispherand **45**, and consequently, it has been necessary to design the monomer further.

Table 2.12. Chemical shifts of the inner and the outer methoxy protons for hemispherand 45, monomer 28, and poly(hemispherand) polymer 52

	Chemical shift, δ in ppm	
	inner $-OCH_3$	outer $-OCH_3$
Hemispherand **45**[a]	2.56	3.39
Monomer **28**	3.20	3.49
Poly(hemispherand) **52**	3.15 (cyclic units)	3.42
	3.20 (pendant units)	

[a] Ref. 28.

2.7 Conclusion

Cyclopolymerization is a direct method to prepare polymeric crown ethers. The divinyl ethers such as 1,2-bis(2-vinyloxyethoxy)benzene and 2,2'-bis[2-(2-vinyloxyethoxy)ethoxy]-1,1'-binaphthyl are most suited for the purpose. In this chapter, the diepoxy compound has been newly recognized as a member of the suitable monomer.

The first diepoxide is 1,2-bis(2,3-epoxypropoxy)benzene **25** which was prepared from the condensation of 1,2-benzenediol **29** with 1-chloro-2,3-epoxypropane **30**. Diepoxide **25** was polymerized by cationic and the Vandenberg catalysts, thereby giving the soluble polymers only with the cyclic structures. The constitutional unit corresponded to the benzo[10]crown-3. Polymer **33** showed a low cation-binding ability.

The second diepoxide is 1,2-bis[2-(2,3-epoxypropoxy)ethoxy]benzene **26** which was prepared from 1,2-bis(2-hydroxyethoxy)benzene **39**. Diepoxide **26** gave the polymers with the constitutional unit corresponding to the benzo[16]crown-5. Polymer **41** showed a highest selectivity for K^+ ion.

The third diepoxide is 5,6:14,15-dibenzo-1,2:18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene **27** which gave the polymer with the constitutional unit corresponding to the dibenzo[19]crown-6. The cation-binding of polymer **44** was higher than those of polymers **33** and **41**, though being slightly less than that of the model dibenzo-crown **6**.

The last diepoxide is 2,6-bis[3-(4,5-epoxy-2-oxapentyl)-2-methoxy-5-methylphenyl]-4-methylanisole **28** with a view of synthesizing the polymer which is composed of the 19-membered hemispherand as the cyclic constitutional unit. Diepoxide **28** was polymerized with cationic, anionic, and the Vandenberg catalysts. The polymers which were obtained with boron trifluoride etherate and tin(Ⅳ) chloride in dichloromethane and with potassium *tert*-butoxide in dimethylsulfoxide were soluble in benzene, chloroform, and tetrahydrofuran. The mole fraction of cyclic units in polymer **52** was 0.65 to 0.75 as compared with 1.0 in polymers **33**, **41**, and **44**. The unexpected result was caused by some participation of the structural crowd.

The cyclopolymerization of diepoxides is, as a result, a facile method of synthesizing poly(crown ether)s with ether linkages in the polymer backbone. The resulting poly(crown ether)s and poly(hemisperand) acted as hosts in host-guest chemistry.

2.8 Experimental Section

Measurements. ^{1}H NMR spectra were recorded with a Hitachi R90H FT-NMR and a Bruker MSL 400 instrument. ^{13}C NMR and CP/MAS NMR spectra were obtained on a Bruker MSL 400 instrument. IR spectra were obtained on a Jasco A-102 spectrometer and a Shimazu IR-435 spectrometer. UV spectra were recorded on a Jasco 660 UV/VIS spectrophotometer. The molecular weights of the resulting polymers were measured by gel permeation chromatography (GPC) in tetrahydrofuran on a WATERS M45 high-performance liquid chromatography equipped with three polystyrene gel columns (Shodex KF-804F). Vapour pressure osmometer (VPO) also was used to determine a number average molecular weight.

Materials. All chemicals were reagent grade. Air-sensitive reactions were performed under a nitrogen atmosphere. Boron trifluoride etherate (BF_3•OEt_2) and tin(Ⅳ) chloride ($SnCl_4$) were purified by distillation of commercial products under reduced pressure. Potassium hydroxide (KOH) and potassium *tert*-butoxide (*t*-BuOK, 1.0 M solution in tetrahydrofuran) were purchased from Aldrich. Triethylaluminium ($AlEt_3$) was kindly supplied from Toyo Stauffer Chemical Co., Ltd. and used without further purification. Dichloromethane, 1,2-dichloroethane, nitroethane, and dimethyl sulfoxide (DMSO) were purified by the usual methods and distilled over calcium hydride before use for polymerization. Toluene and diethyl ether were distilled from sodium benzophenone ketyl immediately prior to use. Dibenzo[18]crown-6 was prepared by the method of Pedersen.[29]

1,2-Bis(3-chloro-2-hydroxypropoxy)benzene (**31**).[7] In 1 L of round-bottomed flask, 110 g (1 mol) of 1,2-benzenediol (**29**) was soluble into 370 g (4 mol) of 1-chloro-2,3-epoxypropane (**30**), and then piperidine hydrochloride[8] was added to the solution. The solution was permitted to stand for 34 days at room temperature in dark place. An excess of **30** was removed under reduced pressure, and then the residue was distilled under vacuum, bp 180 °C / 0.1-0.01 mmHg, giving a 75% yield (222 g) of **30** as viscous syrups. ^{1}H NMR ($CDCl_3$) δ 3.6 (m, oxymethylene and methine

protons, 6H), 4.02 (s, chloromethylene protons, 4H), 4.13 (s, hydroxy protons, 2H), 6.83 ppm (s, arm, 4H).

1,2-Bis(2,3-epoxypropoxy)benzene (**25**).[7] In a three-neck flask equipped with a stirrer, a drying tube (calcium chloride), a thermometer, and a dropping funnel, 11.2 g (0.2 mol) of KOH and 200 mL of absolute ethanol were placed and the solution was cooled at 0-5 °C by ice-water bath. To this flask, a solution of 29.5 g (0.1 mol) of **31** in 200 mL of absolute ethanol was added slowly through the dropping funnel and then the temperature was kept further for 1 h. The content was filtered to remove potassium chloride. The filtrate was diluted with dichloromethane and washed with water until the water layer turned to neutral. The organic layer was dried with anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The residue was distilled under vacuum, bp 139-159 °C / 0.1 mmHg, then the distillate was recrystallized from ether-hexane to give the white needle crystal of **25** in the yield of 13.4 g (60%). IR (KBr) 915 cm^{-1} (ν_{as} epoxy); ^1H NMR ($CDCl_3$) δ 2.56 (dd, epoxy methylene, 2H), 2.69 (dd, epoxy methylene, 2H), 3.15 (m, epoxy methine, 2H), 3.98 (t, oxymethylene, 4H), 6.73 ppm (s, arom, 4H); ^{13}C NMR ($CDCl_3$) δ 149.15, 115.85, 122.30 (arom. carbons), 70.65 (oxymethylene carbon), 50.27 (epoxy methine carbon), 44.65 ppm (epoxy methylene carbon). *Anal.* Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 65.11; H, 6.40.

1,2-Bis(2-hydroxyethoxy)benzene (**39**).[18] In 500 mL of round-bottomed flask fitted with a mechanical stirrer, a reflux condenser, and a dropping funnel, 64 g (1.6 mol) of sodium hydroxide was dissolved in 150 mL of methanol. To this solution 60 g (0.55 mol) of 1,2-benzenediol (**29**) in 120 mL of methanol was added. The flask was heated under reflux for 10 min after which it was cooled and 126 g (1.6 mol) of 2-chloroethanol was added dropwise. The mixture was heated under reflux for 24 h. The methanol was removed under vacuum and a residue was dissolved with benzene and the insoluble inorganic salt (NaCl) was filtrated. The methanol in the filtrate was evaporated under reduced pressure and then distilled under vacuum, bp 194-204 °C / 0.15 mmHg, giving **39** in a yield of 86.5 g (80%). After recrystallization from benzene, **39** was

obtained as a colorless crystal with a yield of 83.6 g (77%), having mp 86.0-87.0 °C. IR (KBr) 3250 (ν, OH), 1120 and 1250 (ν, ether), 740 (δ arom.) cm^{-1}.

1,2-Bis[2-(2,3-epoxypropoxy)ethoxy]benzene (**26**). The procedure employed combines the method reported by Kuwamura[19] for the condensation of 1-chloro-2,3-epoxypropane (**30**) with alcohols and that by Kharash et al.[20] for the epoxydation of chlorohydrin ethers (**40**). In 500 mL of three-neck flask equipped with a mechanical stirrer, a reflux condenser, and a dropping funnel, 40 g (0.2 mol) of **39** suspended in dried toluene. To the mixture, 0.5 g of $SnCl_4$ was added and 41 g (0.2 mol) of **30** was dropwise within 10 min instantly. The flask was heated at 50 °C for 1 h. Then after cooling to room temperature, the $SnCl_4$ was trapped with potassium carbonate, and the solution diluted with dichloromethane. The dichloromethane solution washed several times with water until the water layer remained neutral. The organic layer was dried with anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The residue **40** was used without further purification.

The crude ether **40** was treated with KOH (22.4 g, 0.4 mol) in absolute ethanol at 0-5 °C to give the diepoxide **26**. By vacuum-distillation, the fraction boiling at 170-190 °C (0.07 mmHg) gave a product (30.3 g), which was crystallized from ether on cooling to 0 °C. Yield: 15.4 g (25%). Mp 39.0-40.5 °C; bp 177-181 °C / $1x10^{-5}$ mmHg. IR (KBr) 3060, 3000, 2940, 2890, 1595, 1505, 1450, 1333, 1255, 1220, 1125, 1050, 930, 912 (epoxy), 858, 840 (epoxy), and 750 cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.62 (dd, 2H), 2.78 (dd, 2H), 3.19 (m, 2H), 3.51 (dd, 2H), 3.78-3.96 (m, 6H), 4.10 (t, 4H), and 6.90 (s, 4H); ^{13}C NMR ($CDCl_3$) δ 121.69, 114.88, 148.94 (arom. carbons), 69.90, 68.86, 71.98 (oxymethylene carbon), 50.81 (epoxy methine carbon), 44.19 ppm (epoxy methylene carbon). *Anal.* Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 61.95; H, 7.25. Exact Mass calcd: 310.3; found: 310 (molecular ion), 57 (glycidyl ion).

5,6; 14,15- Dibenzo- 1,2; 18,19- diepoxy-4,7,10,13,16-pentaoxa-nonadeca-5,14-diene (**27**). A mixture of 1,2;10,11-dibenzo-1,11-dihydroxy-3,6,9-trioxaundeca-1,10-diene hydrate (**42**)[21] (27.2 g, 88.2 mmol), 1-chloro-2,3-epoxypropane **30** (65.3 g, 706 mmol), and piperidine

hydrochloride[8] (0.09 g, 0.78 mmol) was heated at 60 °C for 38 h. The removal of the excess of **30** gave **43** which was used without further purification.

To a stirred solution of absolute ethanol (110 mL) containing KOH (11.9 g, 211.7 mmol) added a solution of **43** (88.2 mmol) in absolute ethanol (110 mL) for 1 h at -10 °C. After this temperature being maintained for 1 h, the precipitated sodium chloride was filtered off, and the alcoholic solution was concentrated. The residue was dissolved in water and extracted with dichloromethane. Recrystallization from methanol gave **27** (5.0 g, 32%) of mp 70.5-71.8 °C. IR (KBr) 3050, 2990 (ν, epoxy), 2920, 2875 (ν, C-H), 1585, 1502, 1445 (ν, C=C), 1253, 1219 (ν_{as}, Ar-O-C), 1121 (ν_{as}, C-O-C), 1020 (ν_{s}, Ar-O-C), 908, 853 (ν_{as}, epoxy), 739 (δ, benzene ring C-H). ^{1}H NMR ($CDCl_3$) δ 2.71 (dd, 2H, epoxy methylene), 2.84 (dd, 2H, epoxy methylene), 3.33 (m, 2H, epoxy methine), 3.90-4.32 (m, 12H, oxy-methylene), 6.92 (s, 8H, arm.). ^{13}C NMR ($CDCl_3$) δ 149.11, 148.72, 122.15, 121.62, 115.4, 114.86 (aromatic carbons), 70.40, 69.95, 68.95 (oxymethylene carbons), 50.29 (methine carbon of epoxy group), 44.70 (methylene carbon of epoxy group). *Anal.* Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.42; H, 6.61.

2,3,4,5,6,7,8,9,10-Tris[1,3-(2-methoxy-5-methylbenzo)]-12, 15,18-trioxacyclooctadeca-2,5,8-triene (**45**). This compound was prepared according to the method reported by Cram et al.[24]

2,6-Bis[3-(4,5-epoxy-2-oxapentyl)-2-methoxy-5-methylphenyl]-4-methyl-anisole (**28**). A mixture of 40 mL of 50 wt % aqueous sodium hydroxide, 40 mL of 1-chloro-2,3-epoxypropane (**30**), and 1 g of tetrabutylammonium hydrogen sulfate was vigorously stirred at room temperature. To the mixture was added 6.9 g (16.4 mmol) of 2,6-bis(3-hydoxymethyl-2-methoxy-5-methylphenyl)-4-methylanisole (**51**) with cooling in ice so that the temperature did not exceed 25 °C. After 5 h, the reaction mixture was poured into an ice/water. The aqueous phase was extracted with dichloromethane. The organic phase was washed with brine, dried with sodium sulfate, filtered, and evaporated under vacuum. The residue was purified by flash chromatography on silica gel (silica gel 60, 230-400 mesh, Merck) with ether / hexane (v/v, 7/3) to give 6.3 g

(72%) of **27** as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, outer $ArCH_3$, 6H), 2.36 (s, 3H, inner $ArCH_3$), 2.64 (dd, J_{gem}=5.1 Hz, J_{trans}=2.7 Hz, 2H, epoxy CH_2), 2.81 (dd, J_{gem}=4.9 Hz, J_{cis}=4.3 Hz, 2H, epoxy CH_2), 3.20 (s, 3H, inner CH_3O), 3.21-3.23 (m, 2H, epoxy CH), 3.49 (s, 6H, outer CH_3O), 3.53 (dd, J_{gem}=11.4 Hz, J_{vic}=5.9 Hz, 2H, $ArCH_2OCH_2$), 3.83 (dd, J_{gem}=11.4 Hz, J_{vic}=3.1 Hz, 2H, $ArCH_2OCH_2$), 4.65 (AB, J_{gem}=11.6 Hz, 2H, $ArCH_2$), 4.69 (AB, J_{gem}=11.6 Hz, 2H, $ArCH_2$), 7.14 (d, J=2.0 Hz, 2H, ArH), 7.16 (s, 2H, ArH), 7.23 (d, J=1.9 Hz, 2H, ArH). *Anal.* Calcd for $C_{32}H_{38}O_7$: C, 71.89; H, 7.16. Found: C, 71.21; H, 7.20.

Polymerization of 25 with $SnCl_4$, BF_3•OEt_2 and $AlBr_3$ (polymer 33). The solvent and **25** were weighed to a glass ampule. The catalyst solution was charged to the ampule at -30 °C. After standing for 48 h at this temperature, the polymers were worked up by precipitation in an excess of methanol and then dried in vacuum.

Preparation of the Vandenberg catalyst. The Vandenberg catalyst was prepared according to the method reported by Vandenberg.[11] The reaction of $AlEt_3$ with water and acetylacetone was carried out in a Pyrex tube fitted with a three-way cock. The tube was purged with dry nitrogen, and diethyl ether (10 mL) was added. To this ether was added $AlEt_3$ (5 mmol, 0.68 mL) and cooled at 0 °C. Then to this solution under stirring, water (2.5 mmol, 45 μL) was added dropwise over 15 min. Acetylacetone (2.5 mmol, 257 μL) was added dropwise, stirring at 0 °C continued for 15 min. The solution was followed by stirring overnight at room temperature. A clear, light-yellow solution was obtained.

Polymerization of 25 with the Vandenberg catalyst. A dried toluene and **25** were charged into an ampule. The ampule was then cooled in liquid nitrogen, evacuated, sealed, and then placed in a constant temperature bath. The polymer was obtained by precipitation in methanol and then dried in vacuum.

Polymerization of 26 with $SnCl_4$, BF_3•OEt_2 and $AlBr_3$ (polymer 41). The polymerization of **26** was carried out as described above.

Polymerization of 26 with the Vandenberg catalyst. The polymerization of **26** using the Vandenberg catalyst was carried out as described above. *Anal.* Calcd for $(C_{16}H_{22}O_6)_n$: C, 61.92; H, 7.15. Found: C, 59.72; H, 7.12.

Polymerization of 27 with ordinary acid catalysts and the Vandenberg catalyst (polymer 44). Polymerization of **27** was carried out with ordinary acid catalysts such as $SnCl_4$ and BF_3•OEt_2 in CH_2Cl_2 at -30 °C, and by the Vandenberg catalyst in toluene. *Anal.* Calcd for $(C_{22}H_{26}O_7)_n$: C, 65.66; H, 6.51. Found for the polymer prepared with $SnCl_4$ catalyst: C, 63.35; H, 6.42.

Polymerizations of 28. The polymerizations of **28** were carried out with BF_3•OEt_2 and $SnCl_4$ in dichloromethane and nitroethane at -30 °C, and with KOH and *t*-BuOK in DMSO at room temperature. For the Vandenberg catalyst, toluene was used as solvent. The resulting polymers were purified by reprecipitation from chloroform-methanol.

Copolymerization of 25 and monoepoxides. The copolymerization of **25** and 2,3-epoxypropoxybenzene (phenyl glycidyl ether, **37**) was carried out with tin(Ⅳ) chloride in dichloromethane at -30 °C. The ^{1}H NMR spectrometer was used to measure the composition determinations from the relative intensities of resonances observed at 6.8 ppm (aromatic protons in polymer **33** unit) and at 2.8 to 4.6 ppm (oxyethylene protons in polymer **33** unit and polymer **38** unit).

Copolymerization of 27 and monoepoxides. The cationic copolymerizations of **27** and monoepoxides were carried out with tin(Ⅳ) chloride in dichloromethane at -30 °C, and the anionic ones with KOH in DMSO at room temperature. The resulting polymers were purified by reprecipitation from chloroform-methanol. The copolymer compositions were determined from the relative peak areas of the phenyl and aliphatic protons in the ^{1}H NMR spectra.

Molar fraction of cyclic structural units (f_c). The molar fraction of cyclic structural units in the polymers was determined from the relative

area ratio of the residual epoxy and the phenyl protons in the ^{1}H NMR spectra.

Cation-binding property.[27,30] A solution of host compound in dichloromethane was vigorously shaken in a culture tube with a solution of alkali hydroxide and picric acid in water. After separating into two phases, the amount of alkali picrate extracted into dichloromethane was determined by measuring absorbance of picrate remaining in aqueous phase at 357 nm on UV-spectrophotometer. Experimental conditions are as follows: [picric acid]=3.5×10^{-5} mol•L^{-1}, [metal hydroxide]=0.1 mol•L^{-1}, [**45**]=3.5×10^{-5} mol•L^{-1}, [polymer **52**]=7×10^{-3} mol•L^{-1}, [polymer **33**]=[polymer **41**]=[polymer **44**]=[**6**]=3.5×10^{-4} mol•L^{-1}. The extraction equilibrium constant (K_{ex}) was calculated according to the equation reported by Frensdorff.[27]

2.9 References and Notes

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3

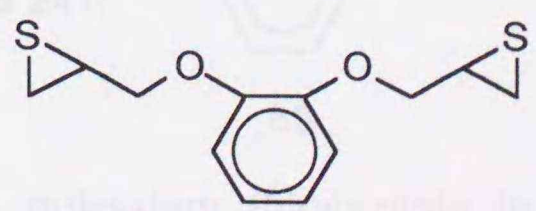
Syntheses of Polymers with Thiacrown Ether Units via Cyclopolymerization of Diepisulfides

Three-membered ring sulfide that is called episulfide or thiirane can be polymerized by modes of anionic, cationic, and coordination polymerization. In 1920, Delepine et al.[1,2] carried out for the first time the polymerization of ethylene sulfide, propylene sulfide, and butylene sulfide with a basic initiator like ammonia, amines, and sodium hydroxide. Marvel[3] and Ohta[4] polymerized propylene sulfide with a basic initiator and obtained a sticky and resinous product in 1954. In case of the ring-opening polymerization of thiiranes, the obtained polymers contain sulfur atoms in these backbone. The polymer is excepted particular properties due to the presence of S atoms. Until recently, however, little practical value was found to the polymers of ethylene and propylene sulfides.

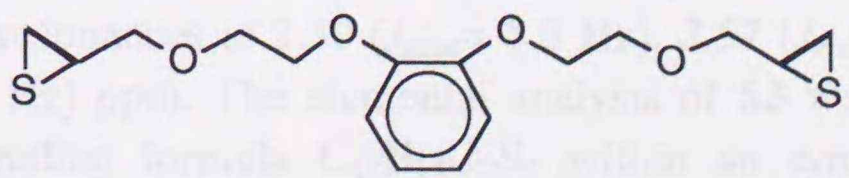
3.1 Cyclopolymerization of Diepisulfides

Various methods have been used to prepare poly(crown ether)s. Polymers with benzo[10]crown-3, benzo[16]crown-5, dibenzo[19]crown-6, and hemispherand units have been synthesized by cyclopolymerization of diepoxides as described in chapter 2. This indicated that cyclopolymerization is a facile method of synthesizing poly(crown ether)s. Polymer with thiacrown ether units containing sulfur atoms also should be obtained by cyclopolymerization of diepisulfides. Because sulfides are characterized as soft donors[5], the thiacrown ethers may combine preferentially with soft acids such as Cu^{2+}, Ni^{2+}, and Cd^{2+}. Therefore, it

Scheme 3.1



53



54

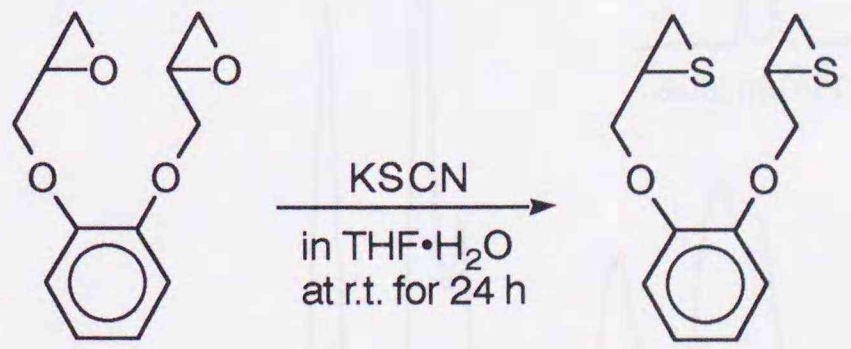
is interesting to see how soft donors affect the cation-binding characteristics of poly(thiacrown ether)s in comparison with those of poly(crown ether)s. Tomoi et al.[6] have reported that poly(thiacrown ether)s can be synthesized via polymer analogous reactions. However, the cyclopolymerization of diepisulfides have not been reported within our knowledge. This chapter treats the cyclopolymerizations of 1,2-bis(2,3-epithiopropoxy)benzene **53** and 1,2-bis[2-(2,3-epithiopropoxy)ethoxy]benzene **54** as indicated in Scheme 3.1, and the cation-binding characteristics of the resulting poly(thiacrown ether)s.

3.2 Synthesis of Poly([10]thiacrown-3)

3.2.1 Preparation of 1,2-Bis(2,3-epithiopropoxy)benzene

Schuetz et al.[7] found a convenient, synthetic method that epoxides are converted into thiiranes by treatment with aqueous alkali thiocyanate, by which a number of unsymmetrically substituted thiiranes were prepared. The procedure employed at this study improves this method by Schuetz (Scheme 3.2). The diepoxide, 1,2-bis(2,3-epoxypropoxy)benzene **25**, in

Scheme 3.2



25 **53**

tetrahydrofuran was treated with a potassium thiocyanate in water at room temperature for 24 h. The corresponding epithio compound **53** was obtained as colourless needles in the yield of 84%. ^{1}H NMR spectrum of **53** showed a typical epithio resonances at 2.30 (J_{gem}= 5.3 Hz), 2.57 (J_{vic}= 3.1 Hz), and 3.29 (J_{vic}= 1.3 Hz) ppm. The elemental analysis of **53** was identified with the corresponding formula $C_{12}H_{14}O_2S_2$ within an error less than 0.09%.

Table 3.1. Polymerization of 1,2-bis(2,3-epithiopropoxy)benzene[a]

Initiator	Solvent	Temp. in °C	Time in h	Yield in %
$SnCl_4$	CH_2Cl_2	-25	48	20.5
	$C_2H_5NO_2$	0	0.2	71.9[b]
$BF_3 \cdot OEt_2$	CH_2Cl_2	-25	48	trace
$AlBr_3$	CH_2Cl_2	-25	48	trace
$Al(i\text{-}Bu)_3\text{-}H_2O$[c]	$C_6H_5CH_3$	0	1.5	17.7
		30	0.5	22.5
		60	0.5	38.0
Vandenberg[d]	$C_6H_5CH_3$	60	24	7.8
		80	24	17.5

[a] [Monomer]=0.5 mol•L^{-1}; [Initiator]=0.05 mol•L^{-1}.
[b] [Monomer]=0.2 mol•L^{-1}; [Initiator]=0.02 mol•L^{-1}.
[c] Triisobutylaluminium / H_2O, molar ratio 2:1.
[d] $AlEt_3$ / H_2O / acetylacetone, molar ratio 2:1:1.

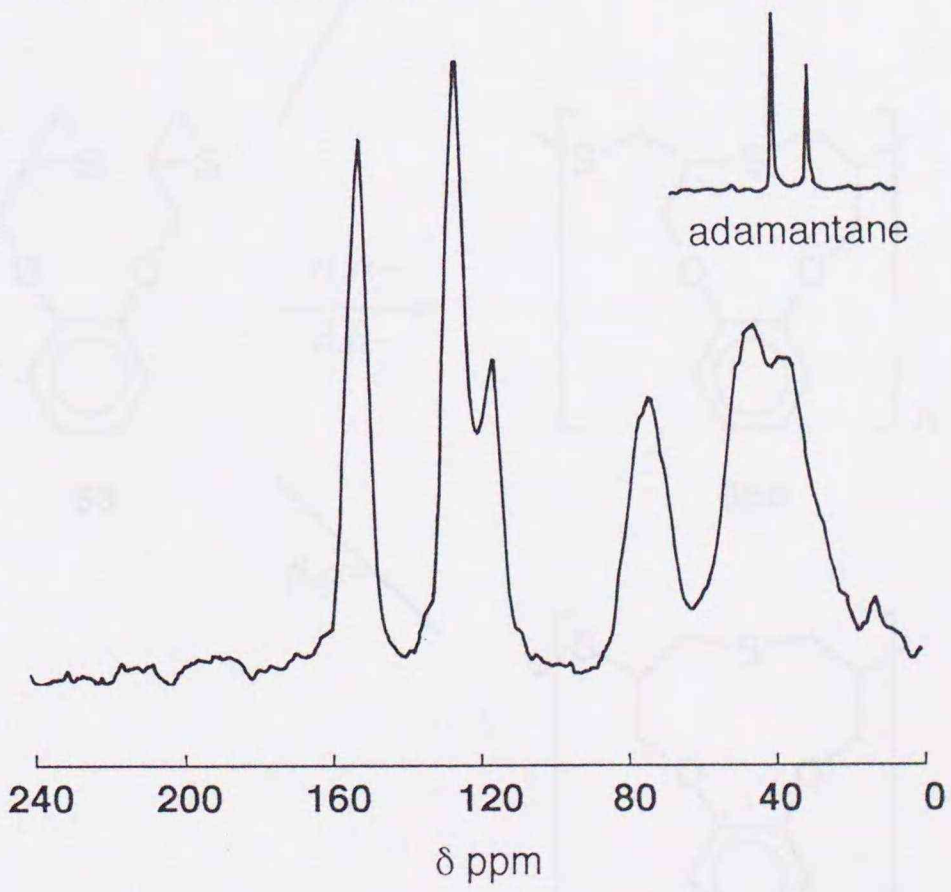


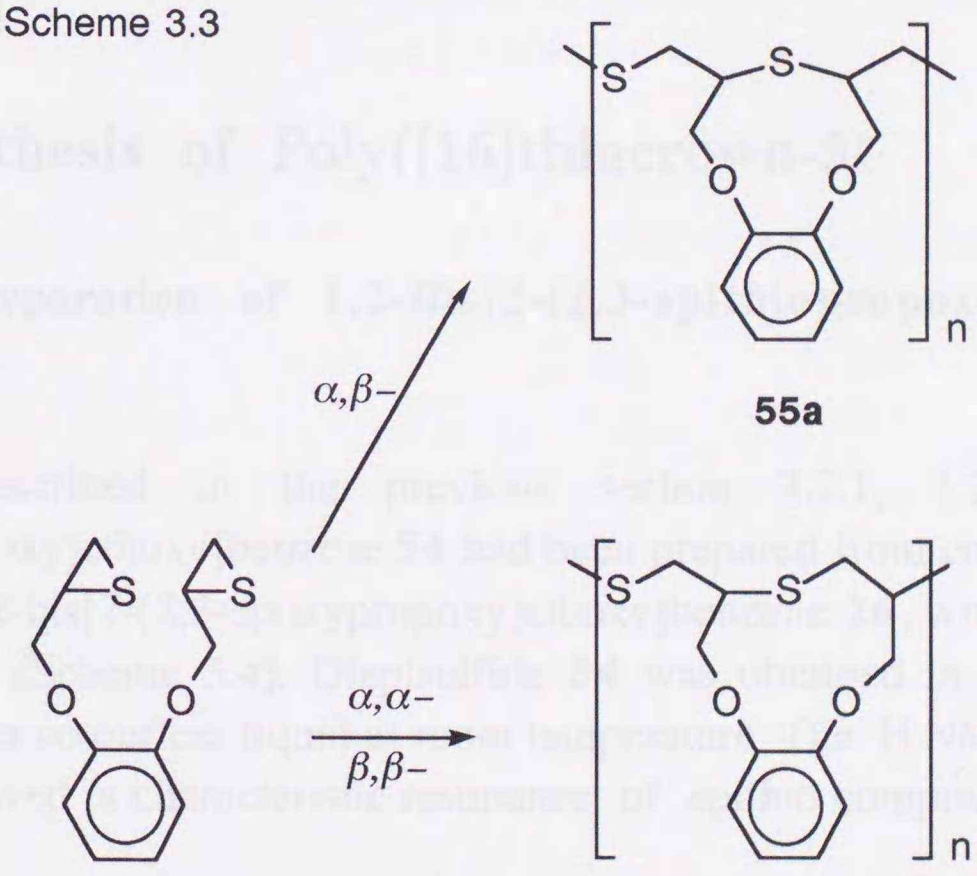
Figure 3.1. High-resolution ^{13}C solid NMR spectrum of polymer 55.

3.2.2 Polymerization of 1,2-Bis(2,3-epithiopropoxy)benzene

Some results of the polymerizations of **53** are given in Table 3.1. Tin(IV) chloride is an active initiator. The Vandenberg[8] catalyst is less effective for the diepisulfide than for the corresponding diepoxide **25**. The triisobutylaluminium catalyst[8] is effective for **53** at relatively high temperatures. The polymers obtained are white powders and insoluble in common organic solvents.

High-resolution ^{13}C solid NMR techniques showed the absence of the episulfide group in the insoluble polymer from **53** (Figure 3.1). Since all episulfide groups participated in the polymerization, the polymers are composed of cyclic constitutional units i.e. thiacrown ether units.

Scheme 3.3



55a **53** **55b** **55c**

3.2.3 Structure of Poly([10]thiacrown-3)

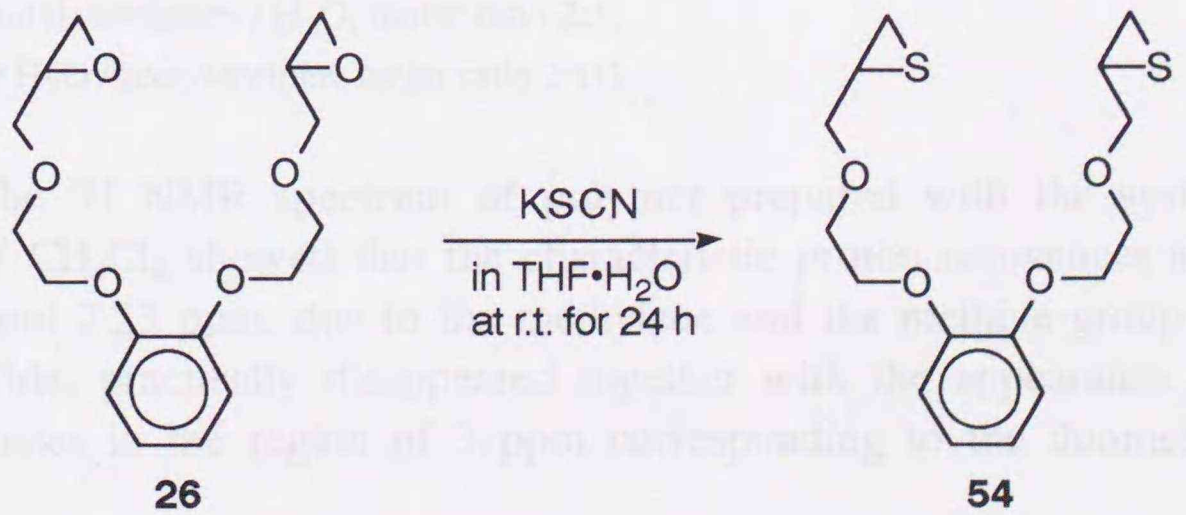
In analogy with the case of epoxide, ring-opening of mono-substituted episulfides occurs in two ways, i.e. by α- or β-scission. In the polymerization of **53** as shown in Scheme 3.3, intramolecular cyclization with α,α- or β,β-scission of two episulfides forms 10-membered rings (polymer **55b**), whereas α,β- and β,α-scission leads to the formation of 9- and 11-membered rings (polymers **55a** and **c**), respectively. Although the polymer obtained represents a mixture of three possible cyclic units, even the random orientation of ring opening gives 50% of benzo-mono-thia[10]crown-3 units, polymer **55b**, as main constitutional units. When the polymerization occurs with some regularity, a dominant fraction of polymer **55b** should be observed.

3.3 Synthesis of Poly([16]thiacrown-5)

3.3.1 Preparation of 1,2-Bis[2-(2,3-epithiopropoxy)ethoxy]-benzene

As described in the previous section 3.2.1, 1,2-bis[2-(2,3-epithiopropoxy)ethoxy]benzene **54** had been prepared from corresponding epoxide, 1,2-bis[2-(2,3-epoxypropoxy)ethoxy]benzene **26**, with potassium thiocyanate (Scheme 3.4). Diepisulfide **54** was obtained in the yield of over 82%, as colourless liquid at room temperature. The ^{1}H NMR spectrum of **54** showed a characteristic resonance of epithio compound at 2.23

Scheme 3.4



26 **54**

(J_{gem}= 5.3 Hz), 2.51 (J_{vic}= 1.0 Hz), and 3.10 (J_{vic}= 1.3 Hz) ppm. The elemental analysis of **54** was identified with the corresponding formula $C_{16}H_{22}O_4S_2$ within an error less than 0.11%.

3.3.2 Polymerization of 1,2-Bis[2-(2,3-epithiopropoxy)-ethoxy]benzene

Some results of the polymerizations are in Table 3.2. Tin(IV) chloride is an active initiator in a similar manner as the polymerization of **53**. The Vandenberg[8] catalyst is less effective for diepisulfides than for diepoxides **26**. Polymers obtained are white powders and insoluble in organic solvents, except that polymer prepared with the system of $SnCl_4$ / CH_2Cl_2 is soluble in *p*-chlorophenol. This soluble polymer had a low molecular weight (intrinsic viscosity $[\eta]$=0.04 in *p*-chlorophenol at 50 °C).

Table 3.2. Polymerization of 1,2-bis[2-(2,3-epithiopropoxy)ethoxy]benzene[a]

Initiator	Solvent	Temp. in °C	Time in h	Yield in %
$SnCl_4$	CH_2Cl_2	-25	2	49.7[b]
BF_3•OEt_2	CH_2Cl_2	-25	2	trace
Al(*i*-Bu)$_3$-H_2O[c]	$C_6H_5CH_3$	60	24	17.7
Vandenberg[d]	$C_6H_5CH_3$	80	24	1.9

[a] [Monomer]=0.5 mol•L^{-1}; [Initiator]=0.05 mol•L^{-1}.

[b] Intrinsic viscosity $[\eta]$=0.04 dL•g^{-1} in *p*-chlorophenol at 50 °C.

[c] Triisobutylaluminium / H_2O, molar ratio 2:1.

[d] $AlEt_3$ / H_2O / acetylacetone, molar ratio 2:1:1.

The ^{1}H NMR spectrum of polymer prepared with the system of $SnCl_4$ / CH_2Cl_2 showed that the characteristic proton resonances at 3.10, 2.51, and 2.23 ppm, due to the methylene and the methine group of the episulfide, practically disappeared together with the appearance of the resonances in the region of 3 ppm corresponding to the thiomethylene

and the thiomethine group as shown in Figure 3.2. Since all episulfide groups participated in the polymerization, polymer **56** is composed of cyclic constitutional units i.e. thiacrown ether units.

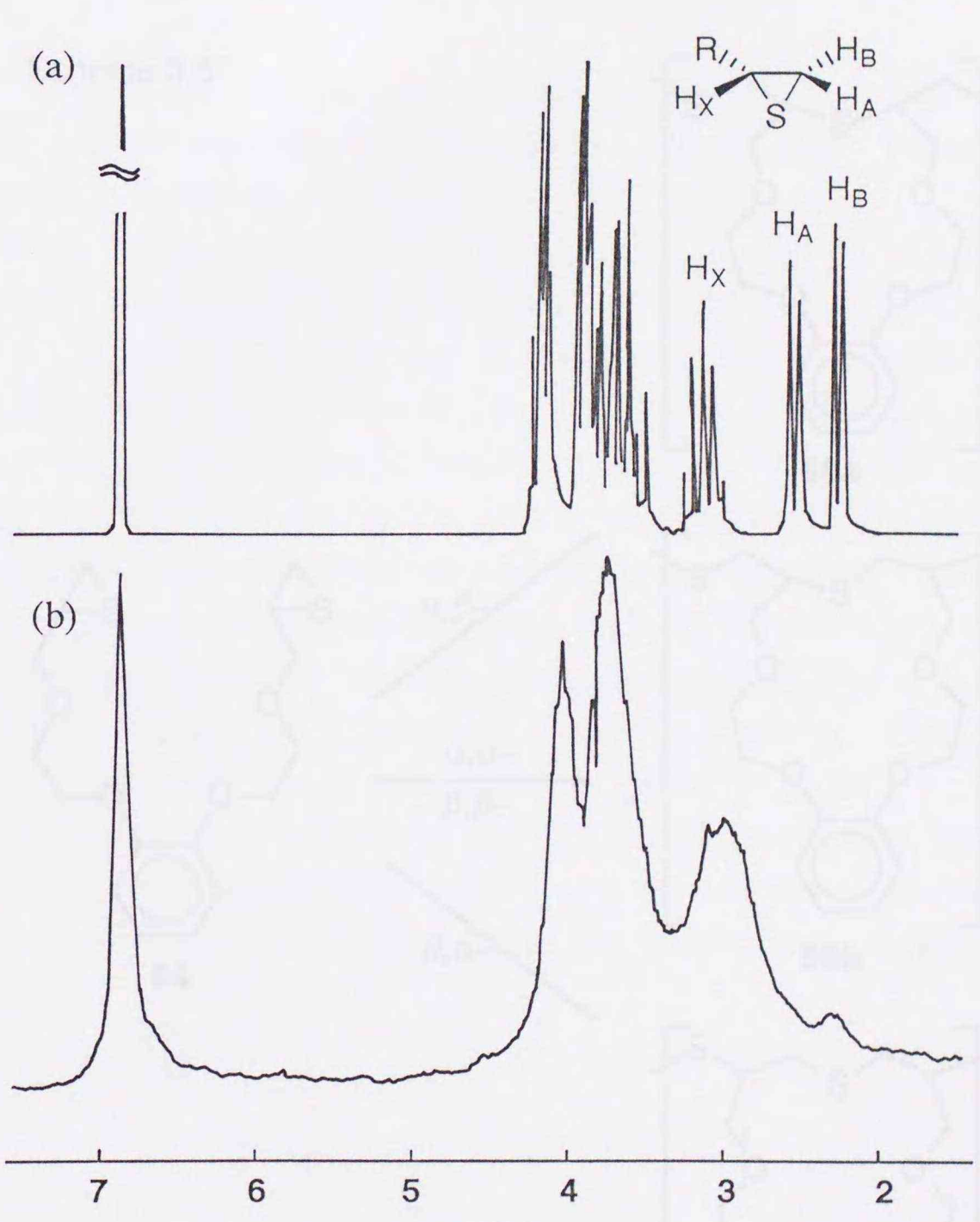
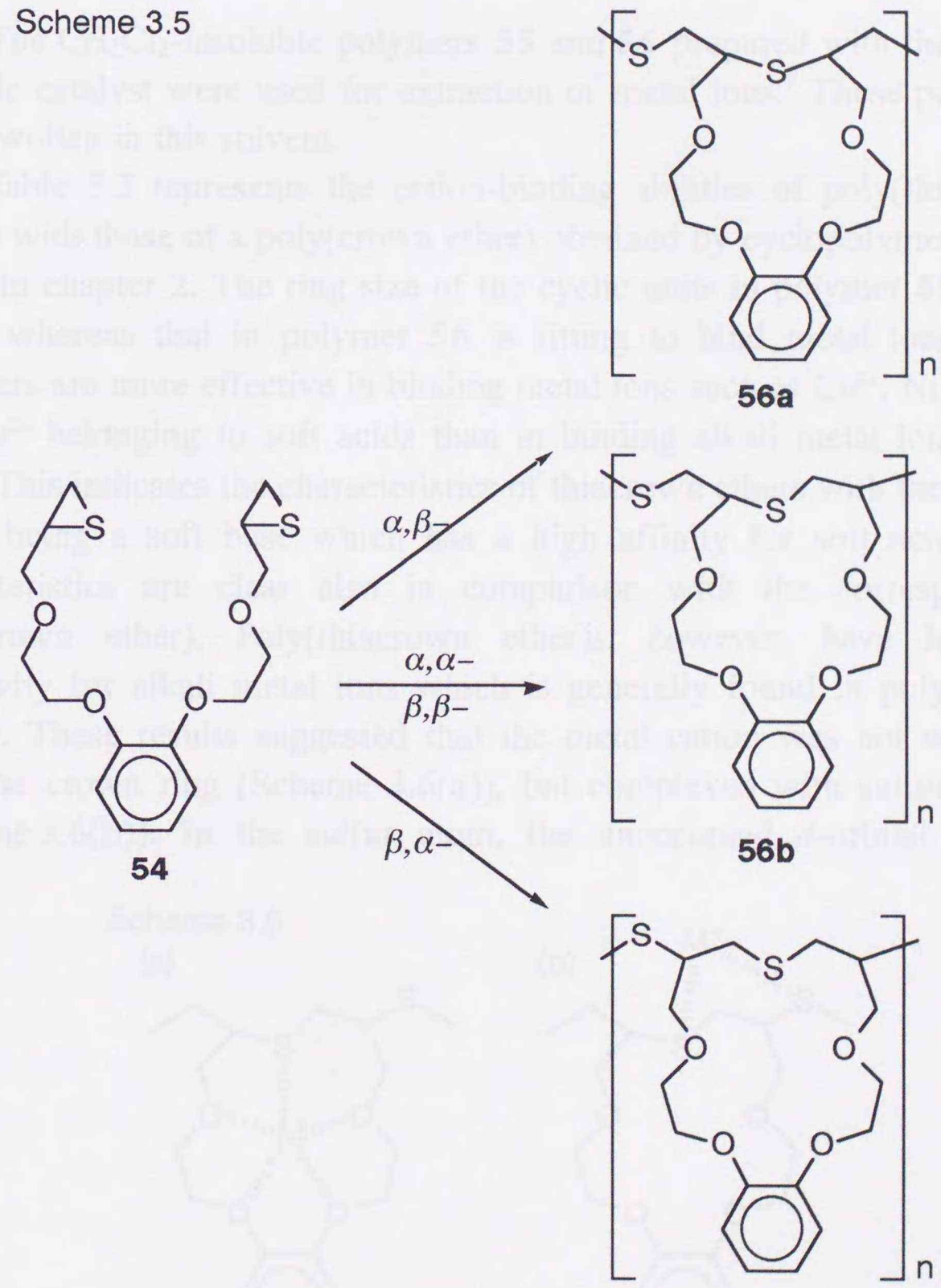


Figure 3.2. ^{1}H NMR spectra of (a) 1,2-bis[2-(2,3-epithiopropoxy)ethoxy]benzene (54) and (b) its polymer 56 prepared with $SnCl_4$ in CH_2Cl_2 at -25 °C.

3.3.3 Structure of Poly([16]thiacrown-5)

In the polymerization of **54** intramolecular cyclization with α,α- or β,β-scission of two episulfides forms 16-membered rings (polymer **56b**), whereas α,β- and β,α-scission leads to the formation of 15- and 17-membered rings (polymers **56a** and **c**), respectively (Scheme 3.5). Although

Scheme 3.5



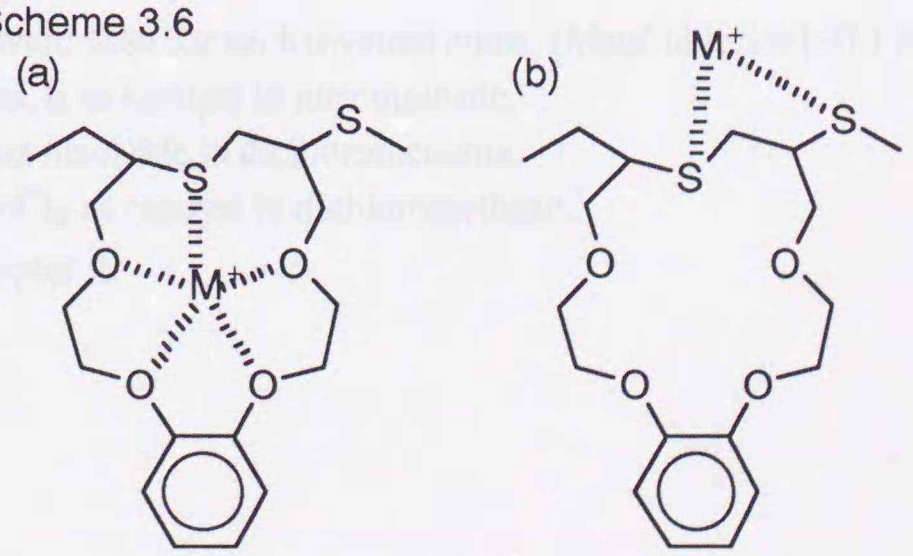
the polymer obtained represents a mixture of three possible cyclic units, even the random orientation of ring opening gives 50% of benzo-mono-thia-[16]crown-5 units, polymer **56b**, as main constitutional units. When the polymerization occurs with some regularity, a dominant fraction of polymer **56b** should be observed.

3.4 Cation-Binding Ability

The CH_2Cl_2-insoluble polymers **55** and **56** prepared with the tin(Ⅳ) chloride catalyst were used for extraction of metal ions.[9] These polymers were swollen in this solvent.

Table 3.3 represents the cation-binding abilities of poly(thiacrown ether)s with those of a poly(crown ether) obtained by cyclopolymerization of **26** in chapter 2. The ring size of the cyclic units in polymer **55** is too small, whereas that in polymer **56** is fitting to bind metal ions. Both polymers are more effective in binding metal ions such as Cu^{2+}, Ni^{2+}, Co^{2+}, and Hg^{2+} belonging to soft acids than in binding alkali metal ions, hard acids. This indicates the characteristics of thiacrown ethers with the sulfide group being a soft base which has a high affinity for soft acids. The characteristics are clear also in comparison with the corresponding poly(crown ether). Poly(thiacrown ether)s, however, have lost the selectivity for alkali metal ions which is generally found in poly(crown ether)s. These results suggested that the metal cation was not wrapped with the crown ring (Scheme 3.6(a)), but complexed with sulfur atoms (Scheme 3.6(b)). In the sulfur atom, the unoccupied *d*-orbital whose

Scheme 3.6



energy level is moderately low has strong interaction with the orbital of the metal ions.

Table 3.3. Extraction of picrate salts by poly[1,2-bis(2,3-epithiopropoxy)benzene] (polymer 55) and poly(1,2-[2-(2,3-epithiopropoxy)ethoxy]benzene) (polymer 56) into the dichloromethane phase[a,b]

Metal ion	Extraction yield in % of the picrates		
	Polymer **55**[c,e]	Polymer **56**[d,e]	Polymer **41**[d,f]
Li^+	3.4	76.3	5.4
Na^+	1.5	78.2	16.2
K^+	1.5	75.0	38.6
Rb^+	1.8	79.2	38.6
Cs^+	4.9	82.6	30.1
Cu^{2+}	24.4	97.9	6.5
Ni^{2+}	20.5	90.3	3.6
Co^{2+}	17.9	87.2	9.7
Cd^{2+}	12.1	89.1	2.2
Hg^{2+}	22.9	54.7	9.7

[a] [Picric acid]=7x10-5 mol•L^{-1}; [Crown units]=3.5x10-3 mol•L^{-1}; [Metal hydroxide]=0.1 mol•L^{-1}.

[b] Metal chlorides were used for each divalent metal, [Metal chloride]=0.1 mol•L^{-1}.

[c] Prepared with $SnCl_4$ as catalyst in nitromethane.

[d] The specimen was insoluble in dichloromethane.

[e] Prepared with $SnCl_4$ as catalyst in dichloromethane.

[f] Table 2.11 in chapter 2.

3.5 Conclusion

In previous chapter 2, the cyclopolymerization of diepoxides is a facile method for synthesizing poly(crown ether)s and poly(hemispherand) with ether linkages in the polymer backbone.

In this chapter, the polymers with thiacrown ether units were synthesized by cyclopolymerization of diepisulfides. The monomers, namely 1,2-bis(2,3-epithiopropoxy)benzene **53** and 1,2-bis[2-(2,3-epithio-propoxy)ethoxy]benzene **54** were prepared from the corresponding epoxides treated with potassium thiocyanate. Diepithio compound **53** was polymerized by cationic and coordination polymerization giving the insoluble polymers. The constitutional unit corresponded to the benzo[10]monothiacrown-3. The polymer **55** showed low cation-binding ability because the ring size of the cyclic unit in the polymer is too small.

A poly(benzo[16]monothiacrown-5) **56** was synthesized from the diepithio monomer **54**. The polymer **56** obtained are white powders and insoluble in organic solvents, except that polymer prepared with tin(Ⅳ) chloride is soluble in *p*-chlorophenol. Since the spectral data indicated the absence of the characteristic proton resonances due to episulfide group, the polymer is composed of cyclic constitutional unit according the cyclopolymerization mechanism. The polymer is fitting to bind metal ions such as Cu^{2+}, Ni^{2+}, Co^{2+}, and Hg^{2+}. This indicates the characteristics of thiacrown ethers with the sulfide group being a soft base which has a high affinity for soft acids.

3.6 Experimental Section

Measurements. ^{1}H NMR spectra were recorded with a Hitachi R90H FT-NMR and a Bruker MSL 400 instrument. ^{13}C NMR and CP/MAS NMR spectra were obtained on a Bruker MSL 400 instrument. IR spectra were obtained on a Jasco A-102 spectrometer and Shimazu IR-435 spectrometer. UV spectra were recorded on a Jasco 660 UV/VIS spectrophotometer.

Materials. Boron trifluoride etherate and tin(Ⅳ) chloride were purified by distillation of commercial reagents under reduced pressure. Potassium hydroxide and potassium *tert*-butoxide (1.0 M solution in tetrahydrofuran) were purchased from Aldrich. Triethylaluminium ($AlEt_3$) was kindly supplied from Toyo Stauffer Chemical Co., Ltd. and used without further purification. Dichloromethane, 1,2-dichloroethane, nitroethane, and dimethyl sulfoxide (DMSO) were purified by the usual methods and distilled over calcium hydride before use for polymerization. Toluene was distilled from sodium-benzophenone. Dibenzo[18]crown-6 was prepared by the method of Pedersen.[10]

1,2-Bis(2,3-epithiopropoxy)benzene (53). The procedure employed improves the method reported by Schuetz et al.[7]: In 100 mL of round-bottom flask, a solution of 2.5 g (11 mmol) of 1,2-bis(2,3-epoxypropoxy)benzene (**25**) in 10 mL of tetrahydrofuran (THF) was added to stirred solution of 6.6 g (68 mmol) of potassium thiocyanate in 8 mL of water at room temperature. As the THF solution was added dropwise, the mixture became heterogeneous. In order to prevent this state, further amounts of THF were added periodically. After 24 h, the solution was extracted with chloroform. The extract was dried with anhydrous sodium sulfate, and the chloroform was removed under vacuum and purified by column chromatography on silica gel (Silica gel 60 MERCK) with chloroform. When the connected chloroform solution evaporated, the residue gave a product which was crystallized from a hexane / ethyl acetate mixture in colourless needles of **53** in the yield of 1.35 g (84%), mp 70-71 °C. ^{1}H NMR ($CDCl_3$) δ 2.30 (dd, 2H), 2.57 (dq, 2H), 3.29 (p, 2H), 3.94 (q, 2H), 4.27 (q, 2H), and 6.92 ppm (s, 4H). *Anal.* Calcd for $C_{12}H_{14}O_2S_2$: C,

56.69; H, 5.52; S, 25.12. Found: C, 56.66; H, 5.55; S, 25.21.

1,2-Bis[2-(2,3-epithiopropoxy)ethoxy]benzene (54). The procedure is similar to that used for **53**, except that the THF solution of 3.2 g (11 mmol) of 1,2-bis(2,3-epoxypropoxy)ethoxy]benzene (**26**) was added to the aqueous solution of potassium thiocyanate under cooling in an ice-bath. The chloroform was removed from the extract, and the residue was purified by column chromatography on silica gel (Silica gel 60 MERCK) with hexane / ethyl acetate (4 / 1), giving a colourless oil of **54** in the yield of 3.1 g (82%). ^{1}H NMR ($CDCl_3$) δ 2.23 (dd, 2H), 2.51 (dq, 2H), 3.10 (p, 2H), 3.48-4.23 (m, 12H), and 6.91 (s, 4H). *Anal.* Calcd for $C_{16}H_{22}O_4S_2$: C, 56.11; H, 6.48; S, 18.72. Found: C, 56.12; H, 6.52; S, 18.61.

Polymerization of 53 and 54. The polymerization were carried out with ordinary acid catalysts, and by the Vandenberg catalyst ($AlEt_3$ / H_2O / acetylacetone, molar ratio 2:1:1[8] and triisobutylaluminium catalyst Al(*i*-Bu)$_3$ / H_2O, molar ratio 2:1.[8]

Cation-binding ability. The extraction of metal picrate was carried out using a similar procedure as the one developed by Pedersen.[9]

3.7 References and Notes

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4

Syntheses of Optically Active Poly(dibenzo[19]-crown-6)s via Cyclopolymerization of Diepoxides

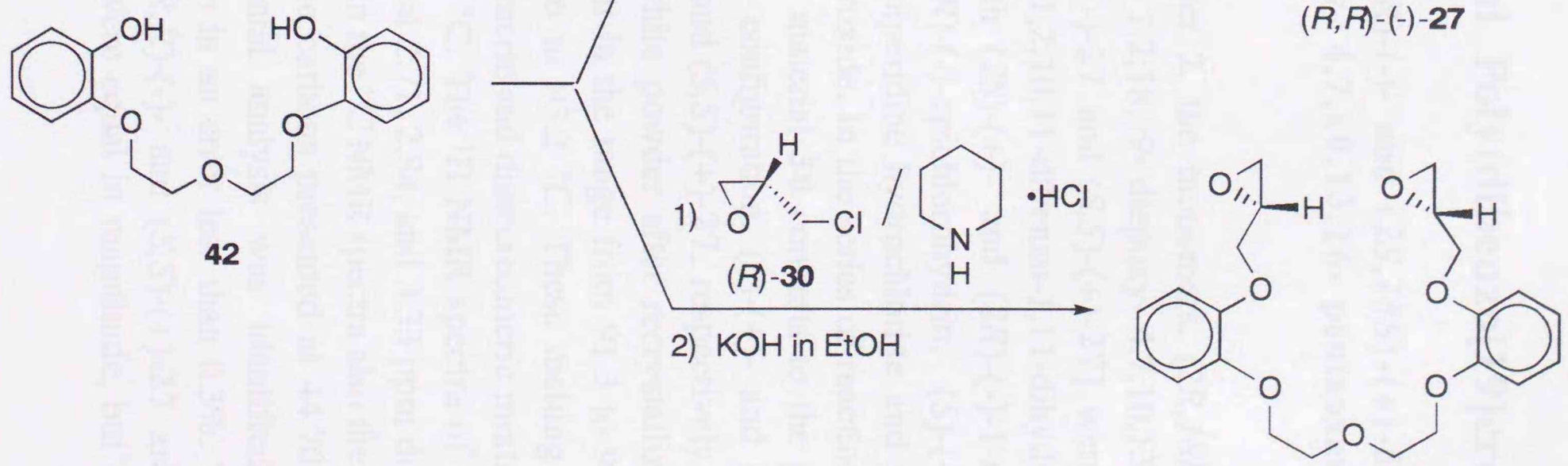
Although chiral crown ethers are important hosts in host-guest chemistry, limited works have reported polymers with chiral crown ether units.[1] Yokota and Kakuchi have established that optically active poly(crown ether)s are easily synthesized through the cyclopolymerization of divinyl ethers incorporating (*R*)- and (*S*)-1,1'-bi-2-naphthol,[2] D-mannitol,[3] L-threitol,[4] and altro-, galacto-, gluco-, and mannopyranosides[5] residues, in which the crown ethers exhibit a chiral recognition ability toward the α-amino acid.

4.1 Cyclopolymerization of Chiral Diepoxides

Optically active macromolecules have been reported to be synthesized by many methods.[6] For the cyclopolymerization system, therefore, suitable designs and controlled polymerizations of bifunctional monomers may produce chiral polymeric crown ethers. In chapter 2, it is described that diepoxide is one of the monomers, as in the case of chiral divinyl ethers, that can be used for the cyclopolymerization forming polymers with crown ether units.[7,8] For example, optically inactive 5,6:14,15-dibenzo-1,2:18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene [(±)-**27**] was polymerized with anionic, cationic and the Vandenberg catalysts to yield polymers with dibenzo[19]crown-6 (polymer **44b**) as the main units, and dibenzo[18]crown-6 (polymer **44a**) and dibenzo[20]crown-6 (polymer **44c**) as the minor ones, as shown in Scheme 2.12.[9] The present study then aims at the preparation of polymeric chiral crown ethers through regio- and stereospecific cyclopolymerization of the enantiomerically pure diepoxides.

This chapter is focussed on the preparation of (*R,R*)-(-)-**27** and (*S,S*)-(+)-**27** using chiral 1-chloro-2,3-epoxypropane **30**, as shown in Scheme 4.1, their cyclopolymerization with cationic and anionic initiators, and the stereoregularity, the chiroptical property, and the chiral recognition

Scheme 4.1


OH
HO
O
O
O
O
O
42
1)
Cl
O
H
•HCl
N
H
(S)-30
2) KOH in EtOH
(R,R)-(-)-27
H
1)
O
Cl
•HCl
N
H
(R)-30
2) KOH in EtOH
(S,S)-(+)-27

of the resulting polymers.

4.2 Synthesis of Chiral Poly(dibenzo[19]crown-6)s

4.2.1 Preparation of (*2R,18R*)-(-)- and (*2S,18S*)-(+)-5,6:14,15-Dibenzo- 1,2:18,19- diepoxy- 4,7,10,13,16- pentaoxanonadeca-5,14-diene

Already described in chapter 2, the monomers, (*2R,18R*)-(-)- and (*2S,18S*)-(+)-5,6;14,15- dibenzo- 1,2;18,19- diepoxy- 4,7,10,13,16- pentaoxanonadeca-5,14-diene [(*R,R*)-(-)-**27** and (*S,S*)-(+)-**27**] were prepared by the condensation of 1,2;10,11-dibenzo-1,11-dihydroxy-3,6,9-trioxaundeca-1,10-diene **42** with (*2S*)-(+)- and (*2R*)-(-)-1-chloro-2,3-epoxypropane [(*S*)-(+)- and (*R*)-(-)-epichlorohydrin, (*S*)-(+)-**30** and (*R*)-(-)-**30**] in the presence of piperidine hydrochloride and subsequent ring closure with potassium hydroxide. In the series of reactions with the Walden's inversion, the starting material **30** converts to the product **27** with clear-cut inversion of the configuration. (*S*)-(+)- and (*R*)-(-)-**30**, therefore, resulted in (*R,R*)-(-)- and (*S,S*)-(+)-**27**, respectively.

(*R,R*)-**27** obtained as a white powder after recrystallization from methanol showed a melting point in the range from 91.3 to 92.9 °C and (*S,S*)-**27** in the range from 91.6 to 93.2 °C. These melting points are different from that of the enantiomeric and diastereomeric mixtures (±)-**27** in the range from 70.5 to 71.8 °C. The ^{1}H NMR spectra of (*R,R*)- and (*S,S*)-**27** showed the resonances at 2.71, 2.84, and 3.33 ppm due to epoxy methylene and methine protons. In the ^{13}C NMR spectra also the resonances of epoxy methylene and methine carbons presented at 44.70 and 50.29 ppm, respectively. The elemental analysis was identified with the corresponding formula $C_{22}H_{26}O_7$ in an error less than 0.3%. The optical rotatory dispersion curves of (*R,R*)-(-)- and (*S,S*)-(+)-**27** are shown in Figure 4.1. Both of the curves were equal in magnitude, but opposite in sign in the ultraviolet region.

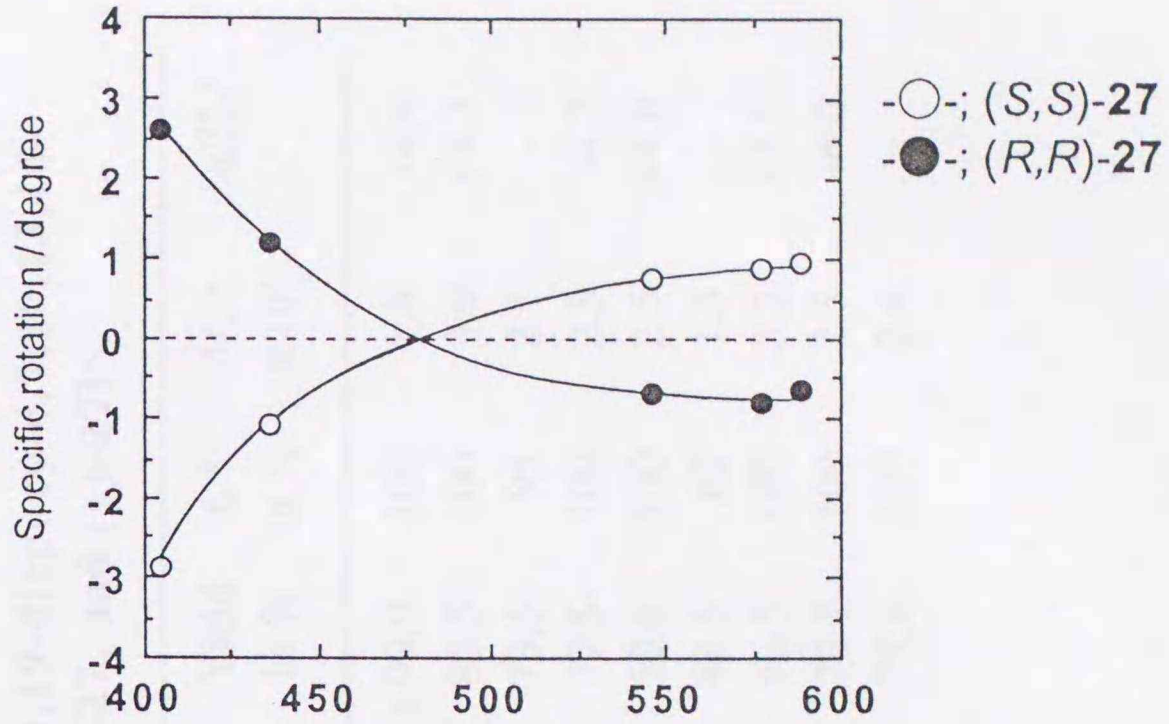


Figure 4.1. Optical rotatory dispersion curves of (*R,R*)-(-)- and (*S,S*)-(+)-27.

4.2.2 Polymerizations of (*2R,18R*)-(-)- and (*2S,18S*)-(+)-5,6:14,15-Dibenzo-1,2:18,19-diepoxy-4,7,10,13,16-pentaoxa-nonadeca-5,14-diene

Some results of the polymerizations of (*R,R*)-(-)- and (*S,S*)-(+)-**27**, and of the enantiomeric and diastereomeric mixture of **27** ((±)-**27**) that was described in chapter 2[9] are listed in Table 4.1. The cationic polymerization of **27** with boron trifluoride etherate and tin(Ⅳ) chloride proceeded homogeneously up to high conversion. The resulting polymers were sticky semi-solid, and soluble in chloroform and tetrahydrofuran. The number-average molecular weight ($\overline{M}_n$) of polymers varied in the range from 1,300 to 3,900. The polymerization of chiral **27** with potassium hydroxide was heterogeneous, while that of (±)-**27** was homogeneous. The powdery polymers obtained were soluble in chloroform but only slightly soluble in tetrahydrofuran; the solubility is different from that of polymers obtained with cationic initiators.

The ^{1}H NMR spectra of (*R,R*)-(-)-**27**, the polymer obtained with potassium hydroxide (polymer **44**(Ⅶ)), and the polymer of (±)-**27** obtained

Table 4.1. Cyclopolymerization of (2*R*,18*R*)-(-)-, (2*S*, 18*S*)-(+)-, and (±)-5,6:14,15-dibenzo-1,2:18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene [(*R*,*R*)-(-)-27, (*S*,*S*)-(+)-27, and (±)-27][a]

Monomer	Initiator (I)	[27] / [I]	Solvent	Temp. in °C	Time in day	Polymer **44**	Yield in %	f_c [b] in %	$\overline{M_n}$ [c] x10^3	$[\alpha]^{25}_{435}$ [d]
(*R*,*R*)-(-)-27	$SnCl_4$	10	Nitroethane	-30	2	I	>99.9	100	1.4	-4.4
(*S*,*S*)-(+)-27						II	85.5	100	3.9	+4.3
(±)-27						III	73.5	95	2.1	-
(*R*,*R*)-(-)-27	BF_3•OEt_2	10	Nitroethane	-30	2	IV	77.5	100	2.5	-4.7
(*S*,*S*)-(+)-27						V	50.8	100	2.5	+4.0
(±)-27						VI	41.5	82	1.3	-
(*R*,*R*)-(-)-27	KOH	5	Dimethyl sulfoxide	r.t.	7	VII	96.5	100	3.2	+5.0
(*S*,*S*)-(+)-27						VIII	78.7	100	2.5	-6.0
(±)-27						IX	79.3	100	2.4	-

[a] [**27**] = 0.5 mol•L^{-1}.

[b] Extent of cyclization in polymer.

[c] Measured in chloroform.

[d] Measured in THF for polymers I-VI and in chloroform for polymers VII-IX.

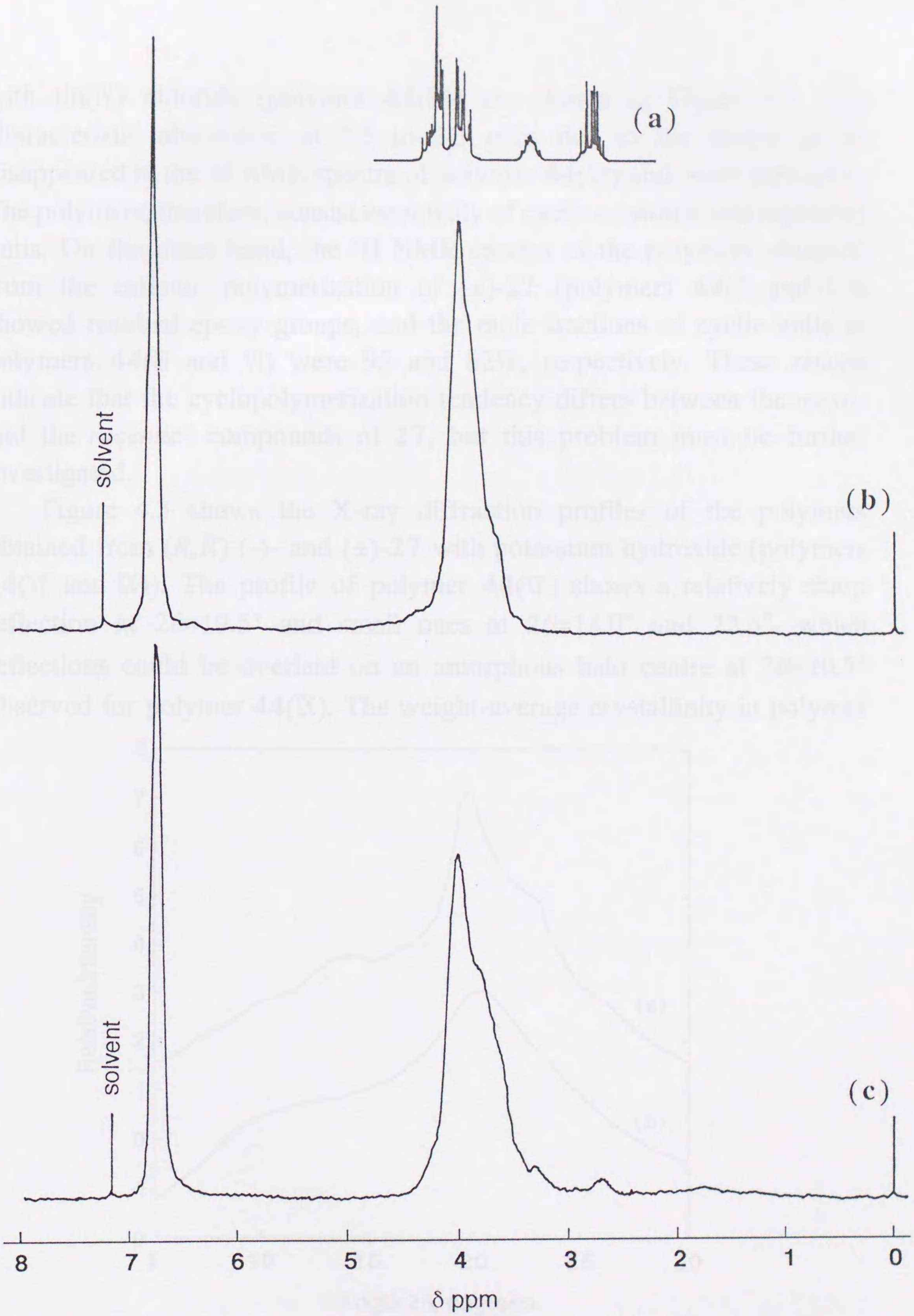


Figure 4.2. ^{1}H NMR spectra of (a) (*R*,*R*)-(-)-27, (b) the polymer obtained with KOH (polymer 44(Ⅶ)), and (c) the polymer of (±)-44 obtained with $SnCl_4$ (polymer 44(Ⅲ)).

with tin(Ⅳ) chloride (polymer **44**(Ⅲ)) are shown in Figure 4.2. The characteristic absorption at 2.5 to 3.3 ppm due to the epoxy group disappeared in the ^{1}H NMR spectra of polymer **44**(Ⅶ) and other polymers. The polymers, therefore, consist essentially of cyclic constitutional repeating units. On the other hand, the ^{1}H NMR spectra of the polymers obtained from the cationic polymerization of (±)-**27** (polymers **44**(Ⅲ and Ⅵ)) showed residual epoxy groups, and the mole fractions of cyclic units in polymers **44**(Ⅲ and Ⅵ) were 95 and 82%, respectively. These results indicate that the cyclopolymerization tendency differs between the *meso*- and the *racemic*- compounds of **27**, but this problem must be further investigated.

Figure 4.3 shows the X-ray diffraction profiles of the polymers obtained from (*R*,*R*)-(-)- and (±)-**27** with potassium hydroxide (polymers **44**(Ⅶ and Ⅸ)). The profile of polymer **44**(Ⅶ) shows a relatively sharp reflection at 2θ=19.5° and small ones at 2θ=14.0° and 22.5°, which reflections could be overlaid on an amorphous halo centre at 2θ=20.5° observed for polymer **44**(Ⅸ). The weight-average crystallinity in polymer

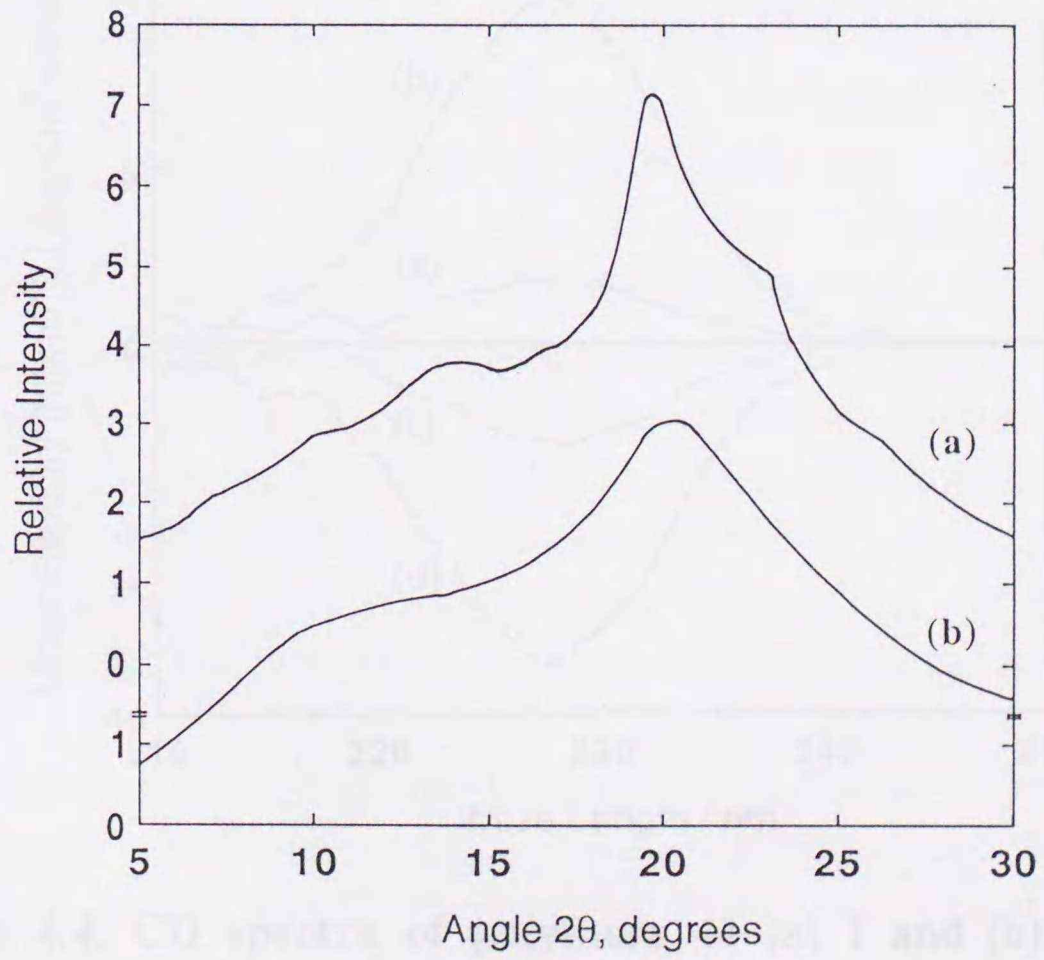


Figure 4.3. X-ray diffraction profiles of polymers 44 (Ⅶ and Ⅸ) obtained from (*R*,*R*)-(-)-27 and (±)-27 with KOH.

44(Ⅶ), which is calculated on the basis of the ratio between the integral intensities of the crystalline and amorphous scattering, was found to be 21 wt%. The crystallinity in polymer **44**(Ⅶ) was also confirmed by the differential scanning calorimetry measurement in which a sharply endothermic peak corresponding to a melting point was observed at 129 °C. These results indicate that (*R,R*)-(-)- and (*S,S*)-(+)-**27** with potassium hydroxide undergo a regio- and stereospecific ring-opening polymerization to produce stereoregular polymers, i.e. mesodiisotactic polymers.

(*R,R*)-(-)-**27** yielded polymers with negative optical rotations ($[\alpha]_{435}^{25}$=-4.4° and -4.7°) by cationic polymerization (polymers **44**(Ⅰ and Ⅳ)), and polymers with positive ones ($[\alpha]_{435}^{25}$=+5.0°) by anionic polymerization (polymer **44**(Ⅶ)). A reverse is shown in the case of (*S,S*)-(+)-**27**, which yielded the polymers with optical rotations of the same absolute values and the reverse sign for each polymerization.

The chiroptical property of the polymeric chain is determined using the CD spectral measurement (Figure 4.4). The CD spectra of polymers

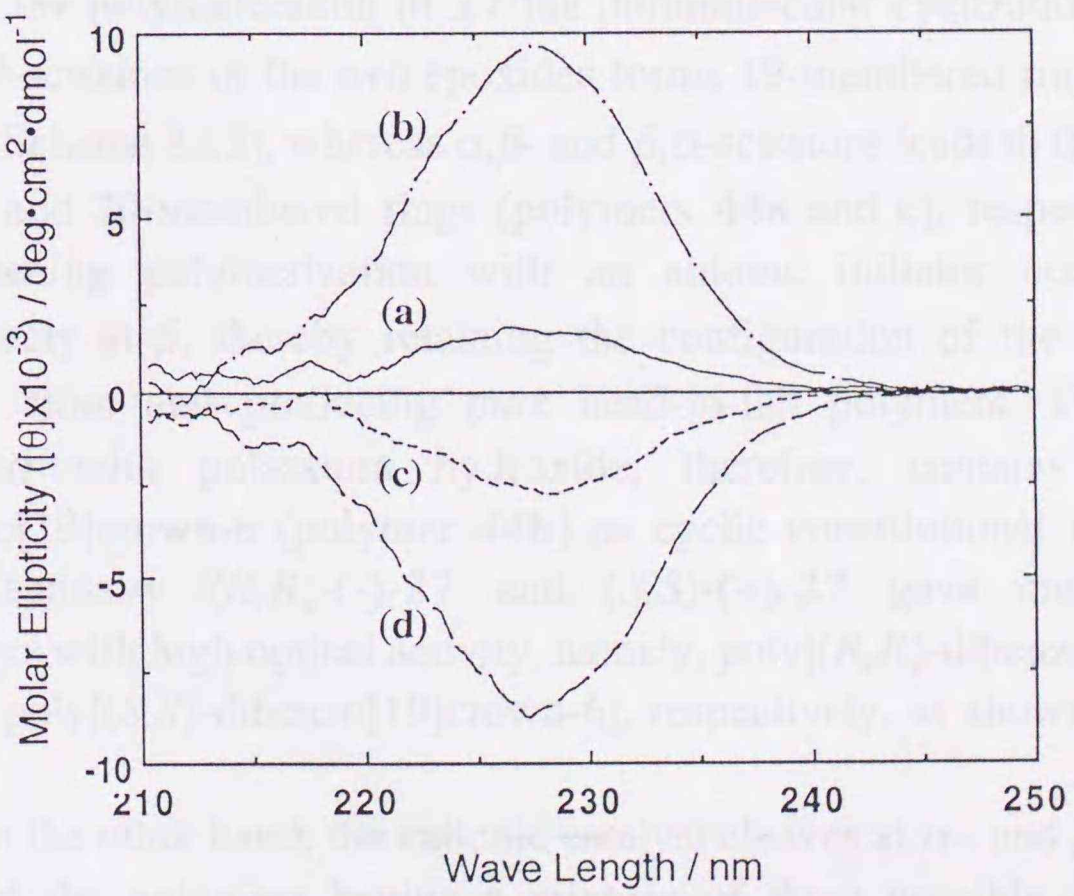


Figure 4.4. CD spectra of polymers 44 (a) Ⅰ and (b) Ⅶ obtained from (*R,R*)-(-)-27 with $SnCl_4$ and KOH, respectively, and polymers 44 (c) Ⅱ and (d) Ⅷ obtained from (*S,S*)-(+)-27 with $SnCl_4$ and KOH, respectively.

from (*R,R*)-(-)-**27** (polymers **44**(I and Ⅶ)) show a positive Cotton effect with a maximum at 228 nm, while the polymers from (*S,S*)-(+)-**27** (polymers **44**(Ⅱ and Ⅷ)) present nearly a mirror image CD curve with a negative Cotton effect. Taking the same sign of the Cotton effect, both polymers, which were obtained by cationic and anionic polymerizations of one enantiomer, should consist of the constitutional units with the same configuration. The absolute values of the molar ellipticity ($[\theta]_{228}^{25}$) for polymers **44**(Ⅶ and Ⅷ) were 3-5 times larger than those for polymers **44**(I and Ⅱ). This means that the polymers obtained with potassium hydroxide have a higher stereoregularity than those with cationic initiators.

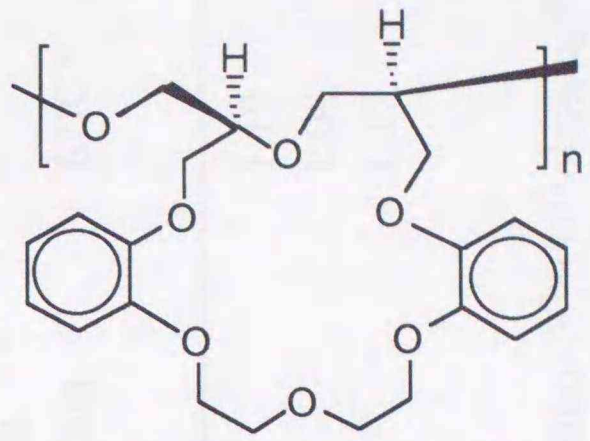
4.2.3 Structures of Poly[(*R,R*)-(+)-dibenzo[16]crown-6)] and Poly[(*S,S*)-(-)-dibenzo[16]crown-6)]

The polymerization of monosubstituted epoxides proceeds through ring-opening at the CH-O and/or the CH_2-O bonds (α- and β-bonds).[10] During the polymerization of **27** the intramolecular cyclization with α,α- and β,β-scissions of the two epoxides forms 19-membered rings (polymer **44b** in Scheme 2.12), whereas α,β- and β,α-scissions leads to the formation of 18- and 20-membered rings (polymers **44a** and **c**), respectively. The ring-opening polymerization with an anionic initiator occurs almost exclusively at β, thereby retaining the configuration of the asymmetric carbon atom and producing pure head-to-tail polymers. The polymer prepared with potassium hydroxide, therefore, contains essentially dibenzo[19]crown-6 (polymer **44b**) as cyclic constitutional units. In the stereochemistry (*R,R*)-(-)-**27** and (*S,S*)-(+)-**27** gave mesodiisotactic polymers with high optical activity, namely, poly[(*R,R*)-dibenzo[19]crown-6] and poly[(*S,S*)-dibenzo[19]crown-6], respectively, as shown in Scheme 4.2.

On the other hand, the cationic catalyst cleaves at $\alpha-$ and $\beta-$ positions to yield the polymers having a mixture of three possible cyclic units, (polymers **44a**, **b**, and **c**). The random orientation of ring-opening forms the main constitutional units with at least 50% of polymer **44b**. The polymers obtained with cationic initiators, in fact, possessed an optical activity, although lower than that for polymers with potassium hydroxide.

Scheme 4.2

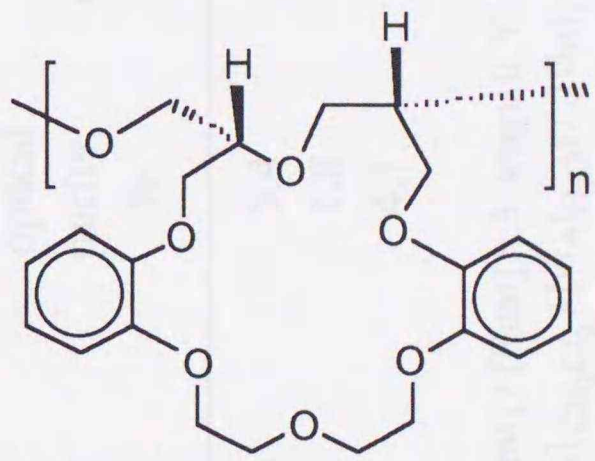
(*R*,*R*)-(-)-**27** ⟶



Poly[(*R*,*R*)-dibenzo[19]crown-6]

Polymer (*R*,*R*)-**44**

(*S*,*S*)-(+)-**27** ⟶



Poly[(*S*,*S*)-dibenzo[19]crown-6]

Polymer (*S*,*S*)-**44**

This means that the ring-opening occurs predominantly at the β-bond to form (*R*,*R*)-dibenzo[19]crown-6 or (*S*,*S*)-dibenzo[19]crown-6 as the main cyclic units.

4.3 Chiral Poly(dibenzo[19]crown-6)s in the Host-Guest Complexation

Table 4.2 lists the results of the chiral recognition property of host polymers **44**(Ⅱ and Ⅶ) which were prepared from (*S*,*S*)-(+)-**27** with tin(Ⅳ) chloride and potassium hydroxide, respectively, towards methyl esters of phenylglycine ($PhGlyOCH_3$), phenylalanine ($PhAlaOCH_3$), and methionine ($MetOCH_3$) as guests. For estimating the chiral recognition ability, the enantiomer distribution constant (EDC) is defined as EDC = $([G_A]_{CH_2Cl_2} / [G_A]_{H_2O}) / ([G_B]_{CH_2Cl_2} / [G_B]_{H_2O})$, where $[G_A]_{CH_2Cl_2}$ and

Table 4.2. Chiral recognition ability of host polymers (*S*,*S*)-44 (Ⅱ and Ⅷ) towards racemic guest $RCH(CO_2CH_3)NH_3^+ \cdot PO_6^-$ [a]

	Ⅱ			Ⅷ		
	Guest in CH_2Cl_2 phase			Guest in CH_2Cl_2 phase		
R	optical purity, %	dominant configuration	EDC [b]	optical purity, %	dominant configuration	EDC [b]
Ph	1.6	D	1.04	5.4	D	1.19
$PhCH_2$	0.5	D	1.06	1.8	D	1.08
$CH_3SCH_2CH_2$	2.0	D	1.07	4.7	D	1.17

[a] [Host] = 0.2 mol•L^{-1} in CH_2Cl_2; [Guest] = 1.0 mol•L^{-1} in H_2O; [Guest] / [Host] = 3; temp, 0 °C.

[b] The enantiomer distribution constant (EDC) is defined as $EDC=([G_A]_{CH_2Cl_2} / [G_A]_{H_2O}) / ([G_B]_{CH_2Cl_2} / [G_B]_{H_2O})$, where $[G_A]_{CH_2Cl_2}$ and $[G_B]_{CH_2Cl_2}$, $[G_B]_{H_2O}$ and $[G_A]_{H_2O}$ are the concentration of the more (A) or less (B) soluble guest enantiomers in the CH_2Cl_2 phase, and the concentration in the water phase, respectively.

$[G_B]_{CH_2Cl_2}$ and $[G_B]_{H_2O}$ and $[G_A]_{H_2O}$ are the concentration of the more (A) or less (B) soluble guest enantiomers in the CH_2Cl_2 phase and the concentration in the water phase, respectively.[11]

The excess enantiomer of guest extracted into the CH_2Cl_2 phase was the D-isomer for every host-guest system, which means that (*S,S*)-dibenzo[19]crown-6, the main units in both polymers, form the complex predominantly with D-enantiomer. The optical purities of guests were undoubtedly low with values ranging from 0.5 to 5.4%, and the maximum value of the enantiomer distribution constant (EDC) was obtained as 1.19 for the polymer **44**(Ⅷ)-PhGlyOCH$_3$ system. The EDC values for every guest were higher for polymer **44**(Ⅷ) than for polymer **44**(Ⅱ). This result is reflected by the fact that the stereoregularity, i.e. the molar ratio of (*S,S*)-[19]crown-6 unit, is higher for polymer **44**(Ⅷ) than for polymer **44**(Ⅱ).

4.4 Conclusion

Chiral diepoxides, (2*R*,18*R*)-(-)- and (2*S*,18*S*)-(+)-5,6: 14,15-dibenzo-1,2:18,19-diepoxy-4,7,10,13,16-pentaoxanonadeca-5,14-diene [(*R,R*)-(-)-**27** and (*S,S*)-(+)-**27**], were synthesized enantiomerically, and polymerized with a Lewis acid and KOH. All the polymers obtained were soluble in $CHCl_3$, and consisted essentially of cyclic repeating units. The CD spectra of polymers from (*R,R*)-(-)-**27** showed a positive Cotton effect, while the polymers from (*S,S*)-(+)-**27** presented a mirror image CD curve with a negative Cotton effect. The polymers obtained with KOH possessed higher stereoregularity than those with a Lewis acid. The stereochemistry of polymers from (*R,R*)-(-)-**27** and (*S,S*)-(+)-**27** with KOH were poly[(*R,R*)-dibenzo[19]crown-6] and poly[(*S,S*)-dibenzo[19]crown-6], respectively. Polymers **44**(Ⅱ) and **44**(Ⅷ) obtained from (*S,S*)-(+)-**27** with $SnCl_4$ and KOH, respectively, formed the host-guest complex dominantly with the D-isomer of phenylglycine, phenylalanine, and methionine methyl esters. The optical purities of guests extracted by the both polymers were as low as values ranging from 0.5 to 5.4%. For every host-guest system, the chiral recognition property of polymer **44**(Ⅷ) was higher than that of polymer **44**(Ⅱ).

Although many studies have been reported on the enantioselective

polymerization of racemic epoxides and on the stereoselective polymerization of one enantiomer, the chiral polymers obtained have not found application as agents for the optical resolution of racemates. Optically active glycidol and its derivatives, which are commercially available and are useful for chiral building blocks in organic synthesis, have great potential importance as monomers for producing functional polymers. In the present study, the regio- and stereospecific polymerizations of chiral diepoxides, (*R,R*)-(-)- and (*S,S*)-(+)-**27**, successfully react to yield poly[(*R,R*)-dibenzo[19]crown-6] and poly[(*S,S*)-dibenzo[19]crown-6], respectively, which exhibit chiral recognition ability towards racemic α-amino acids.

4.5 Experimental Section

Measurements. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker MSL 400 instrument. UV spectra were recorded on a Jasco 660 UV / VIS spectrophotometer. Optical rotations were made with a Jasco DIP-140 digital polarimeter. CD spectral measurements were carried out at 25 °C in hexafluoroisopropanol (HFIP) with a sample of 0.5 mg / 1 mL using a Jasco J-720 spectropolarimeter. The path length of the cell was 0.1 cm. X-ray diffraction profiles were obtained in a Rigaku-Denki Geigerflex D-3F apparatus with monochromatized Cu Kα radiation. Differential scanning calorimetry was performed with a Seiko SSC 5200 thermal analysis system. 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-804), and in chloroform on a Shodex DS-4 with two columns of Shodex K-801 and K-802.5. The number-average molecular weight ($\overline{M_n}$) was calculated on the basis of a polystyrene calibration.

Materials. (*R*)-(-)- and (*S*)-(+)-1-Chloro-2,3-epoxypropanes (epichlorohydrins) [(*R*)- and (*S*)-**30**] were obtained from Daiso Co., Ltd. and their optical purity are more than 98% ee. Boron trifluoride etherate (BF_3•OEt_2) and tin(Ⅳ) chloride ($SnCl_4$) were purified by distillation of commercial products under reduced pressure. Potassium hydroxide (KOH) was obtained from Kanto Chemical Co., Inc. and used without further purification. Nitroethane and dimethyl sulfoxide were purified by the usual methods and distilled over calcium hydride.

(2*R*,18*R*)-(-)-5,6:14,15-Dibenzo-1,2 :18,19-diepoxy- 4,7,10,13, 16-pentaoxanonadeca-5,14-diene [(*R*,*R*)-(-)-27]. The syntheses of chiral diepoxides [(*R*,*R*)-(-)- and (*S*,*S*)-(+)-**27**] followed the reported procedure for the enantiomeric and diastereomeric mixture of **27** [(±)-**27**] in chapter 2.[9] The reaction of 8.3 g (28.6 mmol) of 1,2:10,11-dibenzo-1,11-dihydroxy-3,6,9-trioxaundeca-1,10-diene (**42**) with 20 g (216 mmol) of (*S*)-(+)-epichlorohydrin [(*S*)-**30**] in the presence of piperidine hydrochloride was carried out at 60 °C, and then the resulting

bischlorohydrin was treated with alcoholic potassium hydroxide at -10 °C to give 5.6 g of (*R,R*)-(-)-**27** (yield, 48%) as a white powder, mp 91.3-92.9 °C. $[\alpha]_D$ = -0.64, $[\alpha]_{577}$ = -0.78, $[\alpha]_{546}$ = -0.68, $[\alpha]_{435}$ = +1.22, $[\alpha]_{405}$ = +2.60. (*c*=1.28 in $CHCl_3$, 24 °C). ^1H NMR ($CDCl_3$) δ 2.71 (dd, 2H, epoxy -CH_2-), 2.84 (dd, 2H, epoxy -CH_2-), 3.33 (m, 2H, -CH-), 3.90-4.32 (m, 12H, -OCH_2-), 6.92 ppm (s, 8H, arom.). ^{13}C NMR ($CDCl_3$) δ 149.11, 148.72, 122.15, 121.62, 115.4, 114.86 (arom.), 70.40, 69.95, 68.95 (-OCH_2-), 50.29 (-CH-), 44.70 ppm (epoxy -CH_2-). IR (KBr) 3050, 2990 (ν, epoxy), 2920, 2875 (ν, C-H), 1585, 1502, 1445 (ν, C=C), 1253, 1219 (ν_{as}, Ar-O-C), 1121 (ν_{as}, C-O-C), 1020 (ν_s, Ar-O-C), 908, 853 (ν_{as}, epoxy), 739 (δ, benzene ring C-H). *Anal.* Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.42; H, 6.54.

(2*S*,18*S*)-(+)-5,6:14,15-Dibenzo- 1,2: 18,19-diepoxy- 4,7,10,13, 16-pentaoxanonadeca-5,14-diene [(*S,S*)-(+)-27]. From 4.2 g (14.3 mmol) of **42** with 10 g (108 mmol) of (*R*)-(-)-**30**, 3.2 g of (*S,S*)-(+)-**27** was obtained as a white powder (yield, 56%). Mp 91.6-93.2 °C. $[\alpha]_D$ = +0.96°, $[\alpha]_{577}$ = +0.87, $[\alpha]_{546}$ = +0.76, $[\alpha]_{435}$ = -1.07°, $[\alpha]_{405}$ = -2.88°. (*c*=1.21 in $CHCl_3$, 28 °C). The ^1H and ^{13}C spectra of (*S,S*)-(+)-**27** was identical with those of (*R,R*)-(-)-**27**. *Anal.* Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.36; H, 6.47.

Polymerizations. The cationic polymerizations were carried out with BF_3•OEt_2 and $SnCl_4$ in nitroethane at -30 °C, and the anionic ones with potassium hydroxide in dimethyl sulfoxide at room temperature. The resulting polymers were purified by reprecipitation from chloroform-methanol.

Mole fraction of the cyclic structural units (f_c). The mole fraction of the cyclic structural units in the polymers was determined from the relative peak areas of the protons in the ^1H NMR spectra.

Chiral recognition toward methyl ester of α-amino acid. The procedure for the chiral recognition of chiral polymers was carried out by a similar experiment to the one reported by Yokota[5]

4.6 References and Notes

(1) (a) Sousa, L. R.; Sogah, G. D. Y.; Hoffmann, D. H.; Cram, D. J. *J. Am. Chem. Soc.*, **1978**, *100*, 4569. (b) Sogah, G. D. Y.; Cram, D. J. *J. Am. Chem. Soc.*, **1979**, *101*, 3035. (c) Manecke, G.; Winter, H. -J. *Makromol. Chem., Rapid Commun.* **1981**, *2*, 569. (d) Fyles, T. M.; McGavin, C. A.; Thompson, D. E. *J. Chem. Soc., Chem Commun.* **1982**, 924.

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5

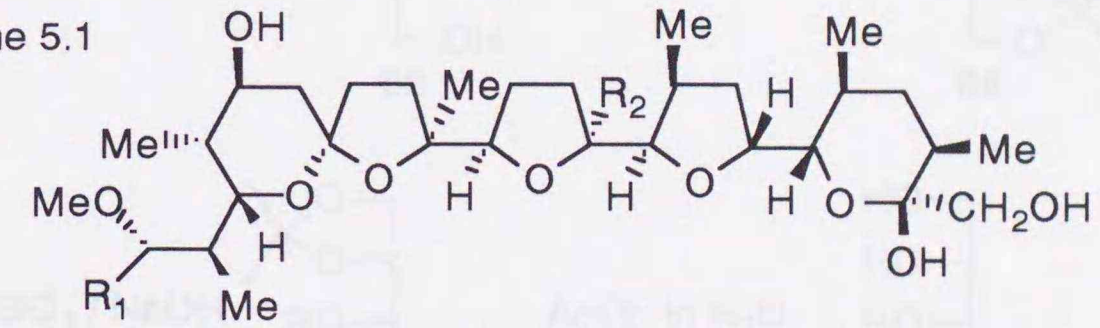
A New Family of Macromolecular Ionophores

Host-guest complexation is an important concept in all the fields of chemistry.[1] A purpose of this study is to establish the synthetic method for host polymers and to clarify their structural properties in complexation. In this chapter the synthesis of macromolecular ionophores via cyclopolymerization of diepoxides[2] is described.

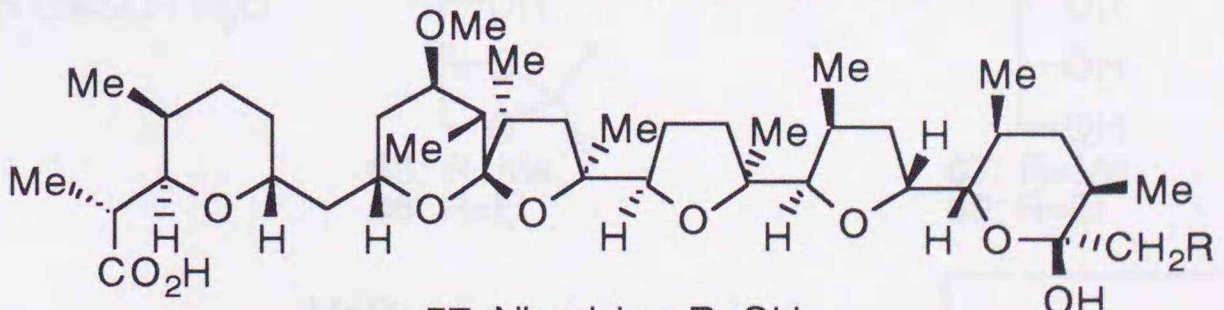
5.1 Ionophores

The naturally occurring ionophores containing polyether antibiotics, such as monensin **12**, nigericin **57**, antibiotic X-206 **58**, and alborixin **59**, are constructed by a formally linear array of tetrahydrofuranyl and tetrahydropyranyl rings as shown in Scheme 5.1. The ionophores form

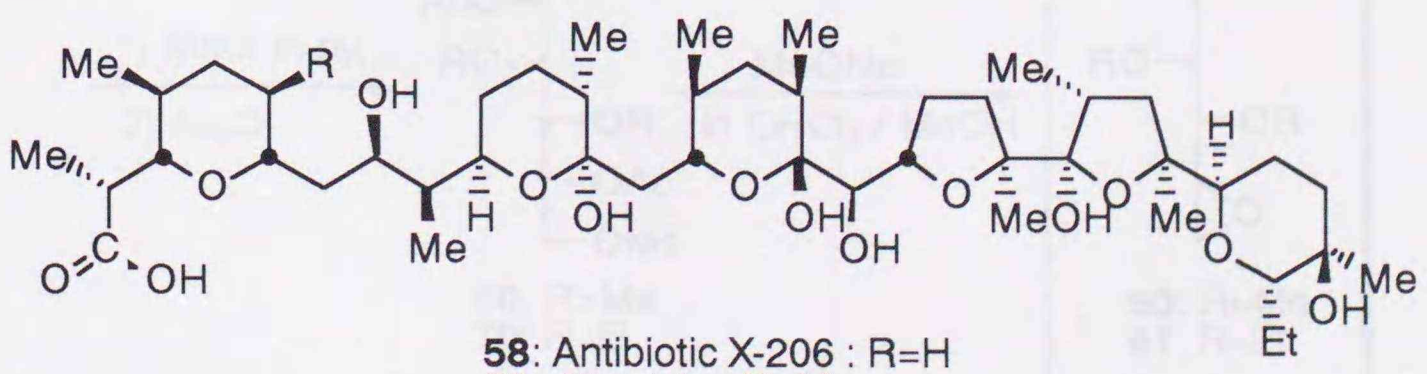
Scheme 5.1



12: Monensin : R_1=CH(Me)CO_2H ; R_2=Et



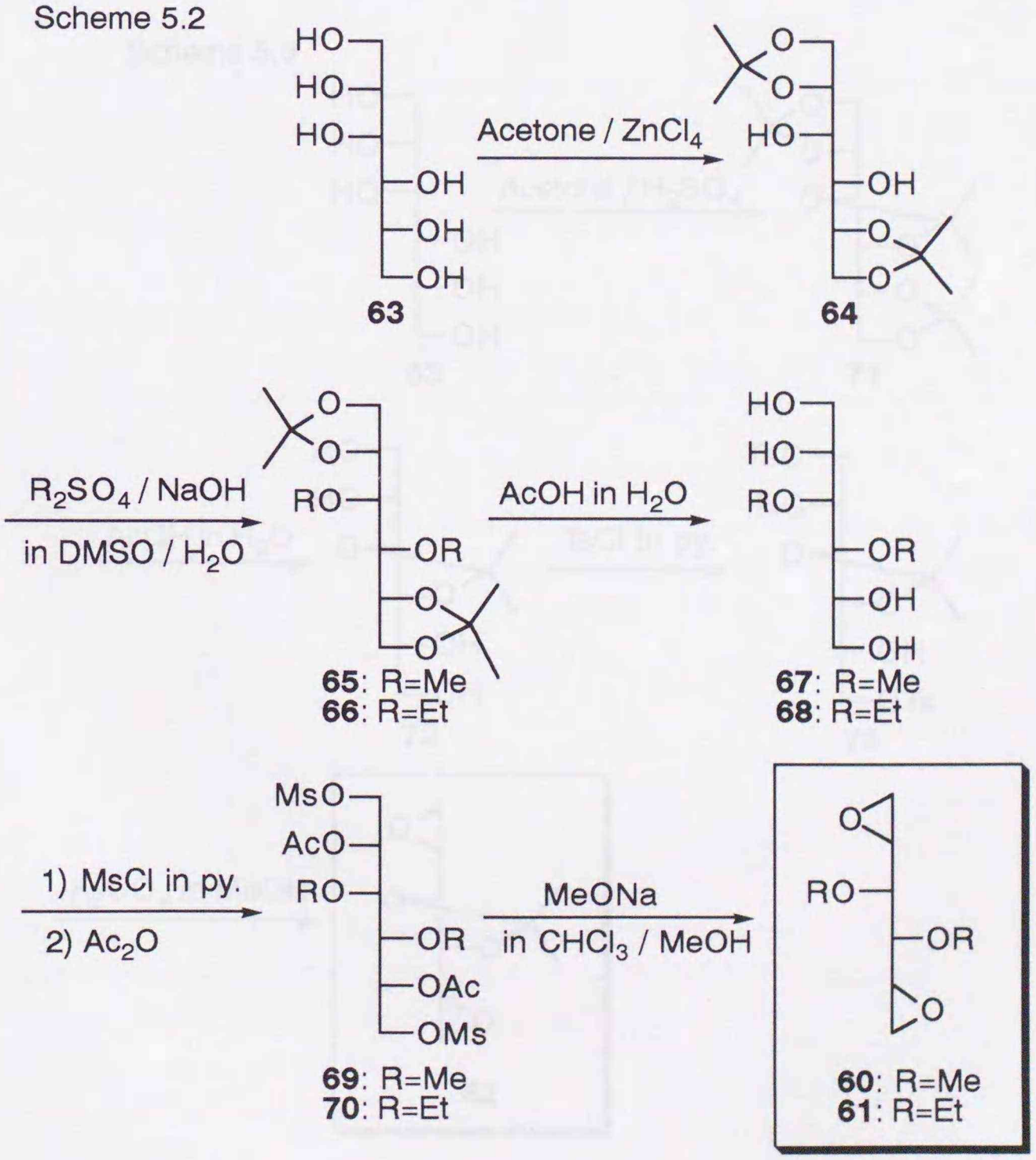
57: Nigericin : R=OH



58: Antibiotic X-206 : R=H
59: Alborixin : R=Me

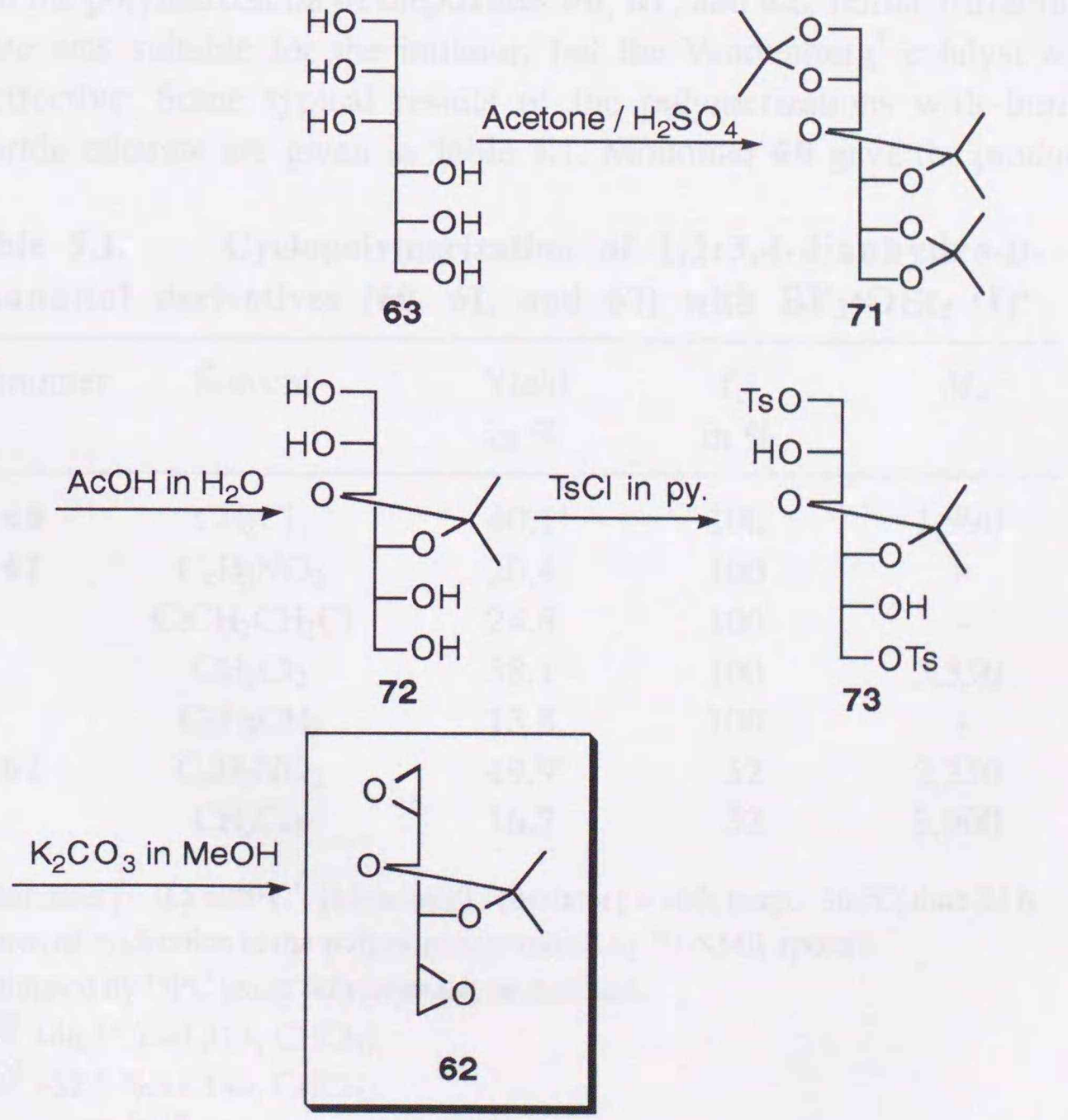
lipophilic complexes with cations, which transport the cations across a membrane. α,ω-Poly(cyclooxalkane)diyl, so-called synthetic polyether ionophore, was synthesized through ring expansion of the oxiranes derived from the polymers of butadiene and cyclopentene by Smith.[3] The obtained polymer, *threo*-α,ω-poly(2,6-tetrahydrofuran)diyl **15**, possessed the binding ability with cations, e.g. Li^+, Ba^{2+} and methylene blue (Scheme 1.8). In addition, poly(7-oxanorbornene) **16** was synthesized through the metathesis polymerization by Grubbs[4], which bound various cations containing methylene blue and rhodamine 6G as shown in Scheme 1.9. Unlike the crown ethers, these acyclic ionophores form helical conformers capable of varying their pitch and cavity size to optimize multidentate

Scheme 5.2



coordination with a given cation. The polymer acting as ionophores must be controlled to have a higher order structure like helical structure. The monomers, 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol **60**[5], 1,2:5,6-dianhydro-3,4-di-*O*-ethyl-D-mannitol **61**[5], and 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol **62**[6] best fit to achieve the purpose of synthesis for polymers containing tetrahydrofuranyl and tetrahydropyranyl rings. D-Mannitol having a C_2-symmetry is a useful unit as chiral element. Diepoxides derived from D-mannitol need not to be distinguished two faces, and consequently give the polymer with the same cyclic unit, in spite of the reaction faces. In particular, diepoxide **62** is prepared for the synthesis of cyclodextrin-like polymer, after the cleavage of isopropylidene as protecting group, forming hydrophobic cavity.

Scheme 5.3



5.2 Syntheses of Macromolecular Ionophores

5.2.1 Preparations of Diepoxides from D-Mannitol

Schemes 5.2 and 5.3 show the derivations of diepoxides from D-mannitol by use of the method reported by Kuszmann[5] and Wiggins[6], respectively. 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-D-mannitol **60** and 3,4-di-*O*-ethyl-D-mannitol **61** were prepared through five steps from D-mannitol, and 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol **62** through four steps.

5.2.2 Polymerizations of Diepoxides Derived from D-Mannitol

In the polymerization of diepoxides **60**, **61**, and **62**, boron trifluoride etherate was suitable for the initiator, but the Vandenberg[7] catalyst was less effective. Some typical results of the polymerizations with boron trifluoride etherate are given in Table 5.1. Monomer **60** gave the product

Table 5.1. Cyclopolymerization of 1,2:3,4-dianhydro-D-mannitol derivatives (60, 61, and 62) with $BF_3 \cdot OEt_2$ (I)[a]

Monomer	Solvent	Yield in %	f_c[b] in %	$\overline{M_n}$[c]
60	CH_2Cl_2	40.1[d]	100	1,990
61	$C_2H_5NO_2$	20.4	100	-
	$ClCH_2CH_2Cl$	24.8	100	-
	CH_2Cl_2	38.1[e]	100	3,350
	$C_6H_5CH_3$	13.8	100	-
62	$C_6H_5NO_2$	49.9[f]	52	2,250
	CH_2Cl_2	16.7	52	3,900

[a] [Monomer] = 0.5 mol•L^{-1}; [Monomer] / [Initiator] = 100; temp. -30 °C; time 24 h.

[b] Extent of cyclization in the polymers determined by ^1H NMR spectra.

[c] Estimated by GPC using poly(styrene) as standard.

[d] $[\alpha]_D^{25}$ +48.1° (*c*=0.313, $CHCl_3$).

[e] $[\alpha]_D^{22}$ +32.7 °(*c*=1.140, $CHCl_3$).

[f] Temp. 0 °C; $[\alpha]_D^{26}$ +10.1° (*c*=1.007, $CHCl_3$).

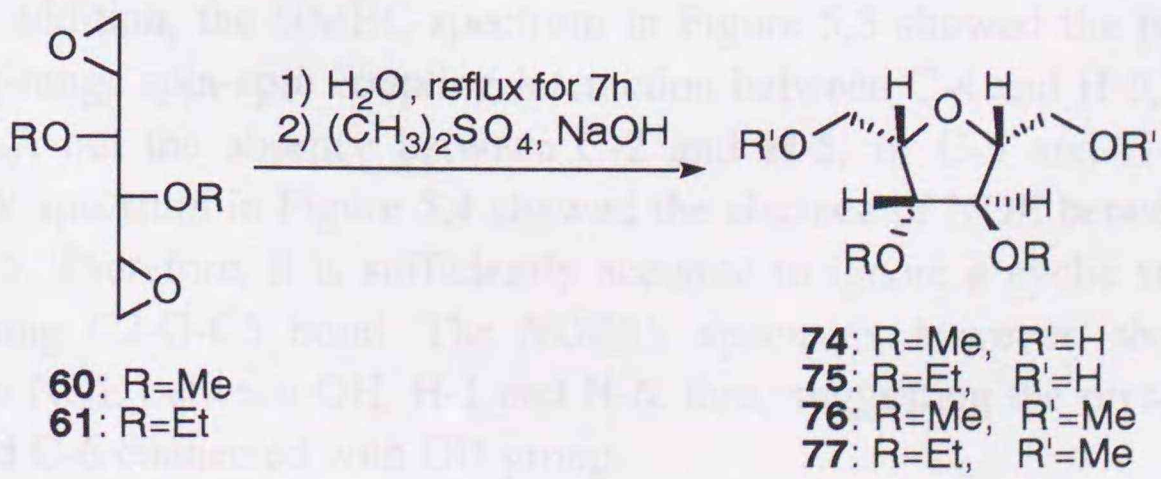
in a 40% yield when polymerized in dichloromethane. The viscous, oily product obtained was optically active with a specific rotation $[\alpha]_D$ of +48.1° (*c*=0.313 in $CHCl_3$). Monomer **61** polymerized in various mediums to give the yield ranging from 13.8 to 38.1%. The products obtained were sticky semi-solids and the one prepared in dichloromethane had a specific rotation $[\alpha]_D$ of +32.7° (*c*=1.140 in $CHCl_3$). The polymerization of monomer **62** gave the product in low yield in dichloromethane at -30 °C, but the powdery one with a specific rotation $[\alpha]_D$ of +10.1° (*c*=1.007 in $CHCl_3$) in reasonable yield in a polar solvent, nitrobenzene, at 0 °C. All the polymers were soluble in chloroform, tetrahydrofuran, and methanol, but insoluble in hexane. The number-average molecular weight ($\overline{M}_n$) of the resulting polymers, which was estimated on the basis of polystyrene standards by means of GPC in THF, was 1,990, 3,350, and 3,900 for polymers **78**, **79**, and **80**, respectively, corresponding to the degree of polymerization in the range of 11 to 18.

5.2.3 Syntheses of Model Compounds

In order to synthesize model compounds for the cyclic structure of the polymers, diepoxides **60** and **61** were hydrolyzed to obtain a monomeric, cyclic compound by the procedure similar to that described by Wiggins[6] for the hydrolysis of 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-hexitols, and followed by the treatment with dimethyl sulfate, as shown in Scheme 5.4.

The hydrolysis of **60** and **61** gave 2,5-anhydro-3,4-di-*O*-methyl-D-mannitol **74** and 2,5-anhydro-3,4-di-*O*-ethyl-D-mannitol **75**, and

Scheme 5.4



60: R=Me
61: R=Et

74: R=Me, R'=H
75: R=Et, R'=H
76: R=Me, R'=Me
77: R=Et, R'=Me

the following methylation gave 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol **76** and 2,5-anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol **77**, respectively.

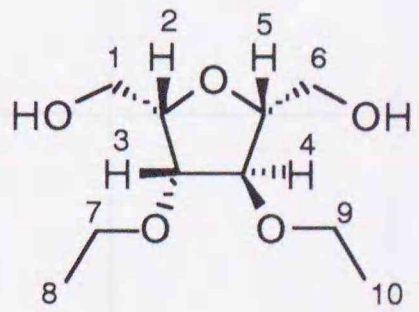
5.2.4 Spectral Assignment and MM Calculation of Model Compounds

Because of lack of anomeric carbon atom, the cyclic model compound showed a complex spectrum in ^{1}H NMR. The hydrogen atom attaching to the anomeric carbon atom is strongly deshielded by two neighboring oxygen atoms and the resonance is shifted to rather downfield. Therefore, the anomeric proton is distinguishable from the other ring-protons.

This section deals with the spectral analysis of the acyclic compound in ^{1}H and ^{13}C NMR with 2D techniques and molecular mechanics of force field (MM calculation), and presents the fundamental data of nonanomeric 2,5-anhydro-sugar.

Figure 5.1 shows the ^{1}H NMR DQF-COSY spectrum of 2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol **75**. The 2D NMR technique should help to assign the signals at δ=3.8-4.0 ppm due to H-6, H-5, H-4, and H-1 protons. The data for chemical shifts and coupling constants are given in Table 5.2. The chemical shifts in ^{13}C NMR were assigned from the HMQC spectrum as indicated in Figure 5.2 together with the experimental data in Table 5.2. Because of lack of the peaks concerning long-range correlation between C-3 and H-7, and C-4 and H-9, the bindings of the mannitol moiety to two ethyl groups were determined as given in Table 5.2. In addition, the HMBC spectrum in Figure 5.3 showed the presence of long-range spin-spin coupling interaction between C-4 and H-9, or C-3 and H-7, but the absence between C-2 and H-5, or C-5 and H-2. The NOESY spectrum in Figure 5.4 showed the absence of NOE between H-2 and H-5. Therefore, it is sufficiently accurate to ignore a cyclic structure containing C2-O-C5 bond. The NOESY spectrum, however, showed a positive NOE between OH, H-1 and H-6, thus, suggesting the presence of C-1 and C-6 connected with OH group.

Scheme 5.5



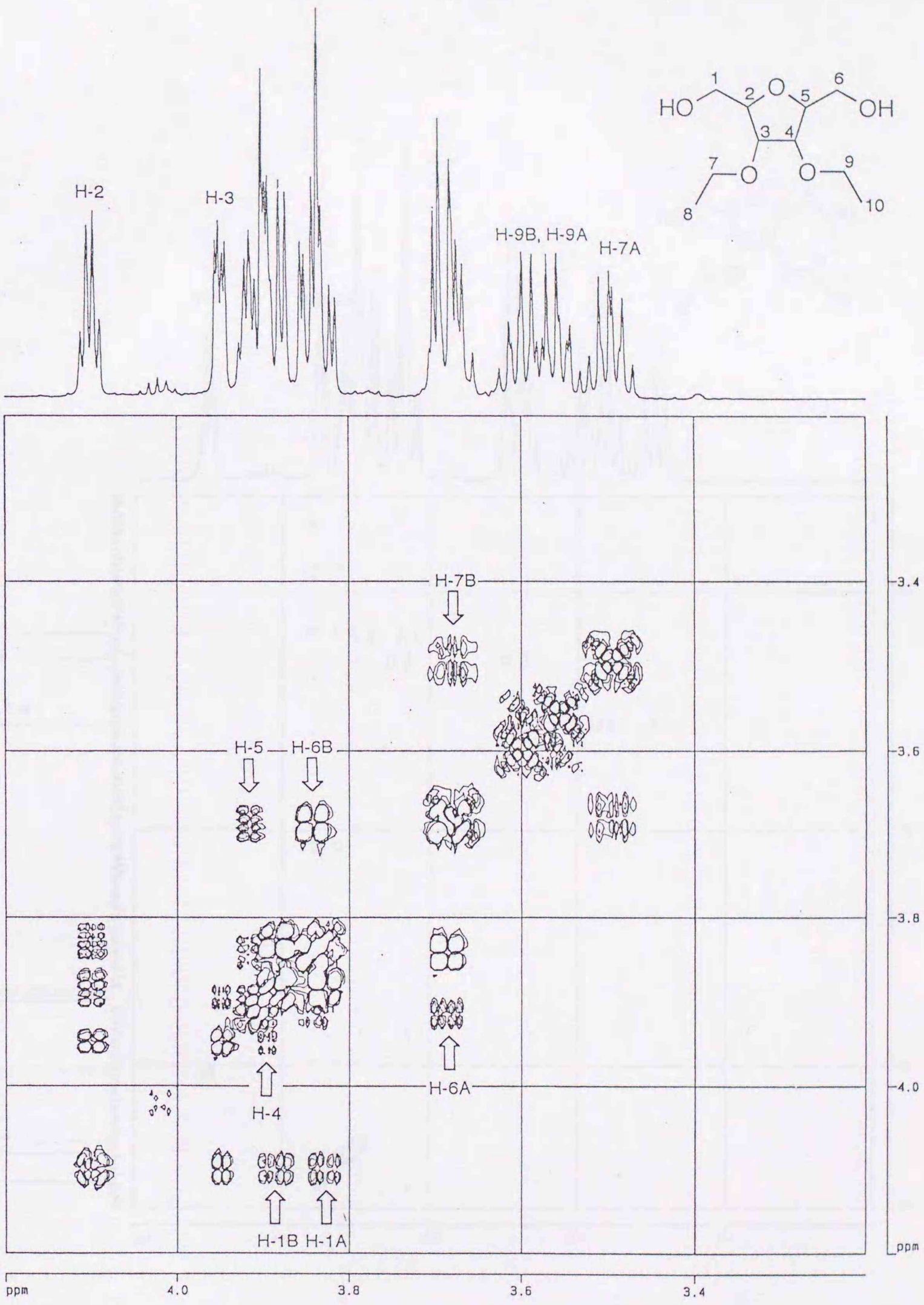


Figure 5.1. Partial ^{1}H NMR DQF-COSY spectrum of 2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol 75.

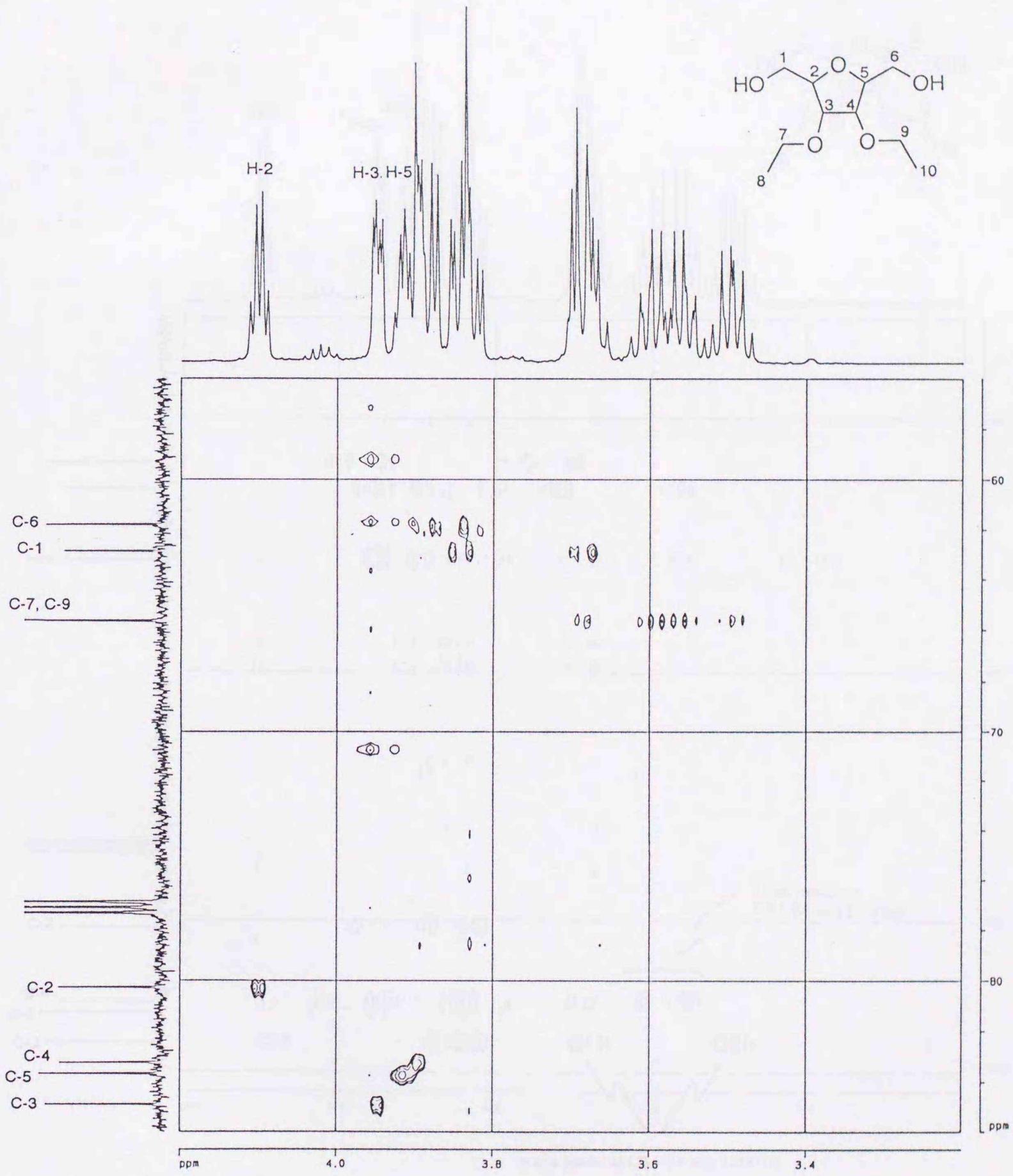


Figure 5.2. Partial HMQC spectrum of 2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol 75.

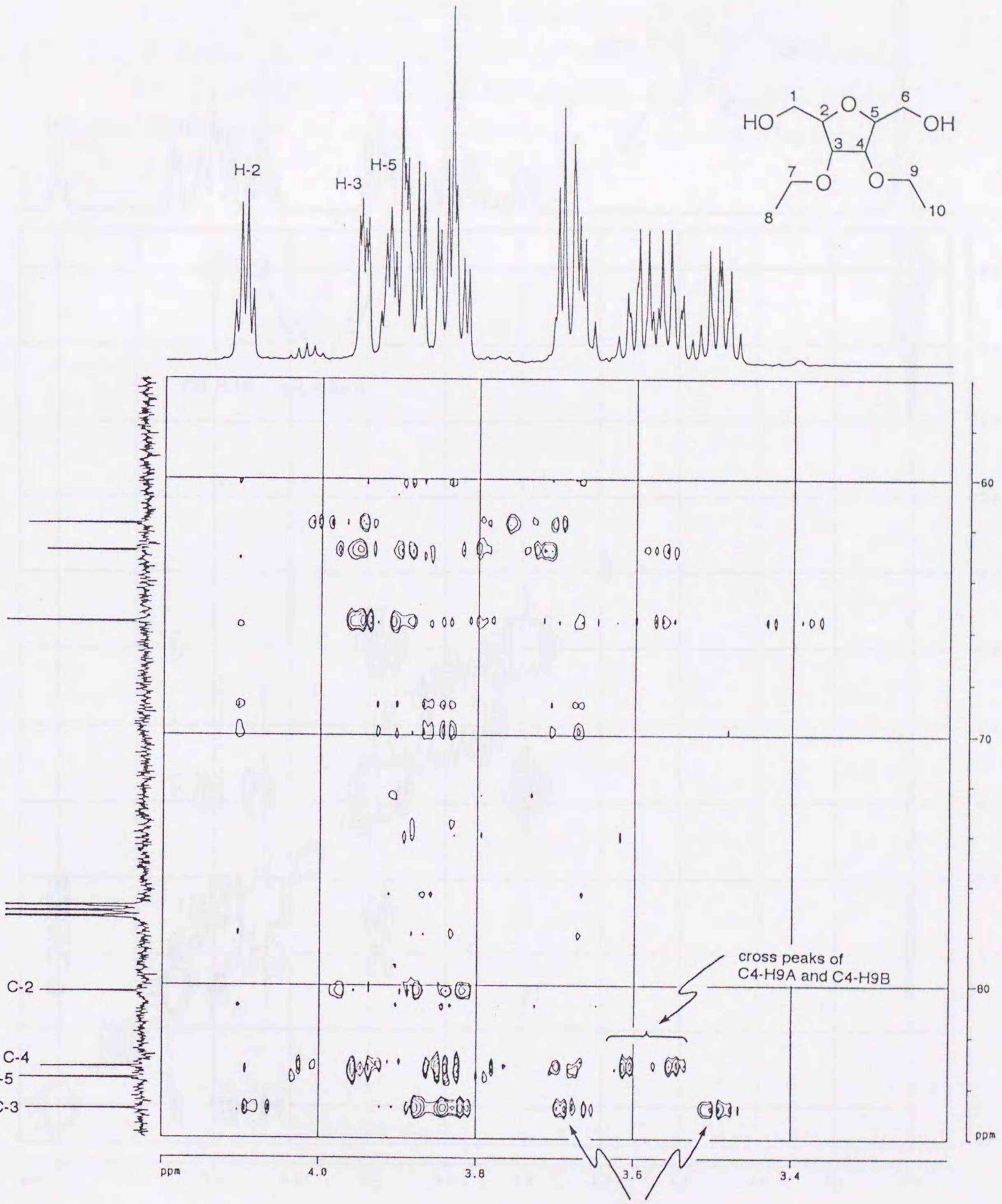


Figure 5.3. Partial HMBC spectrum of 2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol 75.

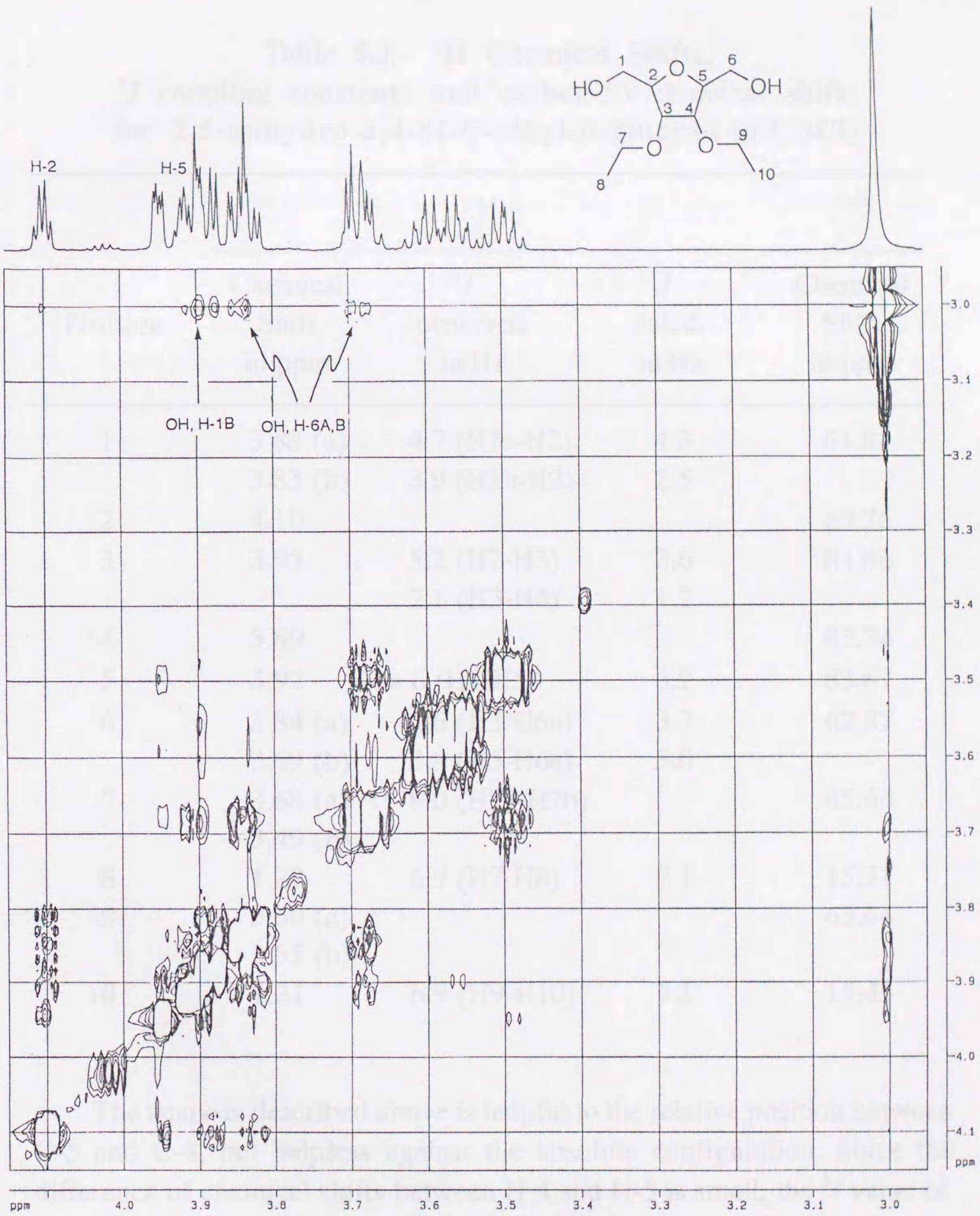


Figure 5.4. NOESY spectrum of 2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol 75.

Table 5.2. ^{1}H Chemical Shifts, ^{3}J coupling constants and carbon-13 chemical shifts for 2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol in $CDCl_3$

	^{1}H			^{13}C
Position	Chemical Shift in ppm	^{3}J observed in Hz	^{3}J calcd. in Hz	Chemical Shift in ppm
1	3.88 (a)	4.7 (H1a-H2)	4.3	61.81
	3.83 (b)	3.9 (H1b-H2)	2.5	
2	4.10			80.26
3	3.95	5.2 (H2-H3)	3.6	84.86
		2.1 (H3-H4)	1.2	
4	3.89			83.24
5	3.92	≅ 6 (H4-H5)	6.2	83.67
6	3.84 (a)	2.6 (H5-H6a)	3.7	62.87
	3.69 (b)	3.9 (H5-H6a)	5.0	
7	3.68 (a)	9.0 (H7a-H7b)		65.64
	3.49 (b)			
8	1.22	6.9 (H7-H8)	7.1	15.31
9	3.60 (a)			65.64
	3.55 (b)			
10	1.21	6.9 (H9-H10)	7.1	15.45

The analysis described above is helpful to the relative position between C-3 and C-4, but helpless against the absolute configuration. Since the difference of chemical shifts between H-4 and H-5 is small, the ^{3}J value of

Scheme 5.6

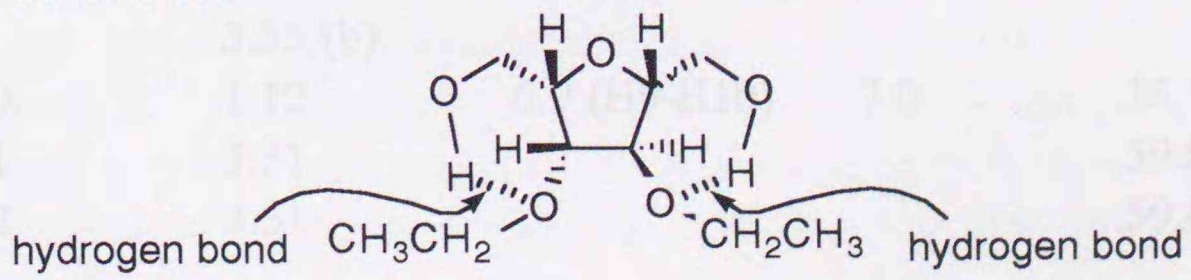


Table 5.3. ^{1}H Chemical shifts, ^{3}J coupling constants and ^{13}C chemical shifts for 2,5-anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol in $CDCl_3$

	^{1}H			^{13}C
Position	Chemical Shift in ppm	^{3}J observed in Hz	^{3}J calcd. in Hz	Chemical Shift in ppm
1	3.41 (a)	5.6 (H1a-H2)	6.0	73.1
		9.9 (H1a-H1b)		
	3.46 (b)			
2	3.85	6.0 (H1a-H2)	6.0	82.2
		6.0 (H1b-H2)	5.0	
		3.4 (H2-H3)	2.1	
3	3.64	3.0 (H2-H3)	2.1	84.3
		< 0.5 (H3-H4)	0.4	
4	3.70	3.9 (H4-H5)	4.0	83.1
		< 0.5 (H3-H4)	0.4	
5	4.04	6.0 (H5-H6a)	4.9	79.7
		4.7 (H5-H6b)	4.1	
		3.9 (H4-H5)	4.0	
6	3.51 (a)	6.9 (H5-H6a)	4.9	70.7
		9.8 (H6a-H6b)		
	3.55 (b)	4.7 (H5-H6b)	4.1	
7	3.45 (a)			64.9
	3.50 (b)			
8	1.13	6.9 (H8-H9)	7.0	15.1
9	3.38 (a)	6.9 (H9a-H10)	7.0	65.0
		9.0 (H9a-H9b)		
	3.55 (b)			
10	1.12	6.9 (H9-H10)	7.0	15.1
11	3.31			59.0
12	3.31			59.0

these protons can not be exactly measured. In order to determine the absolute configuration of **75**, then, the $^{3}J_{HH}$ values were estimated by means of the MM calculation. The observed and calculated values are listed in Table 5.2. The values, which were calculated by considering a hydrogen bond between the OH and OEt groups as shown in Scheme 5.6, are in reasonable agreement with the observed ones.

Figure 5.5 shows the ^{1}H NMR DQF-COSY spectra of 2,5-anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol **77**. The data for chemical shifts and coupling constants are given in Table 5.3. The chemical shifts in ^{13}C NMR were assigned from the HMQC spectra as indicated in Figure 5.6, together with the experimental data in Table 5.3. The configurational relation between two ethyl groups in the sorbitol moiety was estimated by a procedure similar to that used for **75**. The difference of $^{3}J_{H2\text{-}H3}$ (3.9 Hz) and $^{3}J_{H4\text{-}H5}$ (3.0 Hz) is too small to elucidate the absolute configuration. The $^{3}J_{HH}$ values, therefore, were estimated by means of the MM calculation. The observed and calculated values were listed in Table 5.3.

5.2.5 Structural Analysis of the Polymers

Since the ^{1}H and ^{13}C NMR spectra of Figures 5.7 and 5.8 indicated the absence of the epoxy group in polymers **78** and **79**, the polymerization proceeded according to a cyclopolymerization mechanism leading to the polymers with cyclic constitutional repeating units. On the other hand, ^{1}H NMR spectrum of Figure 5.7c showed that the characteristic resonance at δ=2.8 and 3.2 ppm due to the methylene and the methine protons of the epoxide is indicative of a large amount of residual epoxides. The ^{13}C NMR spectrum of Figure 5.8d also brought about the same results. The mole fraction of cyclic structural units (f_c) in the polymers was determined from the relative peak areas of the protons in the ^{1}H NMR spectra. In the polymerization of **62** the maximum of f_c was only 0.5.

The ^{13}C NMR spectrum of polymer **79** showed close agreement with that of **77** (Figure 5.9), and consequently, polymer **79** is essentially composed of the cyclic constitutional unit corresponding to the carbon skeleton of **77**. The similarity of the ^{13}C NMR spectrum of polymer **78** to that of **76** clarified the structure of the polymer as well. The hydrolysis of **62** gave no product consisting of 5-membered ring. Wiggins[6] reported

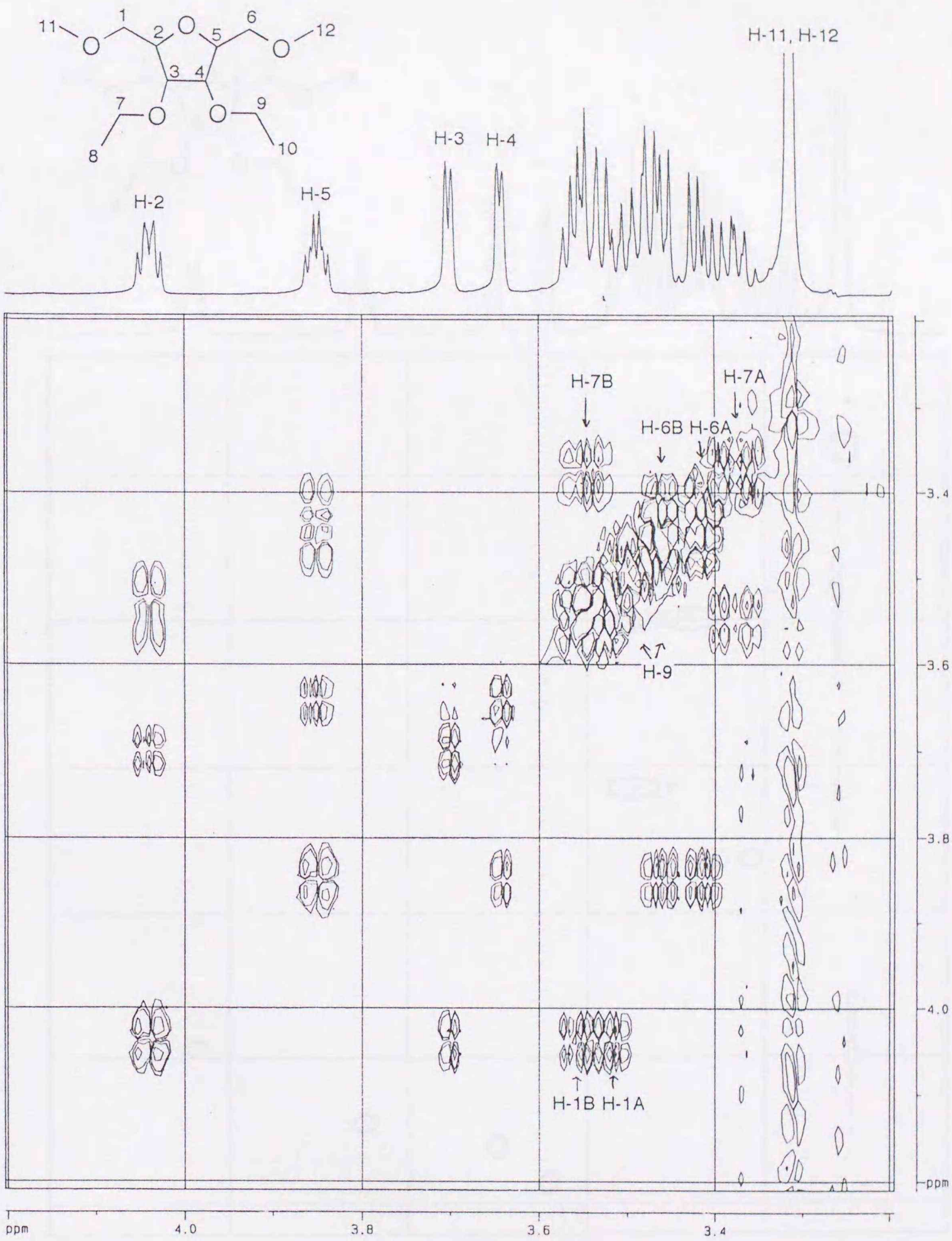


Figure 5.5. Partial ^{1}H NMR DQF-COSY spectrum of 2,5-anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol 77.

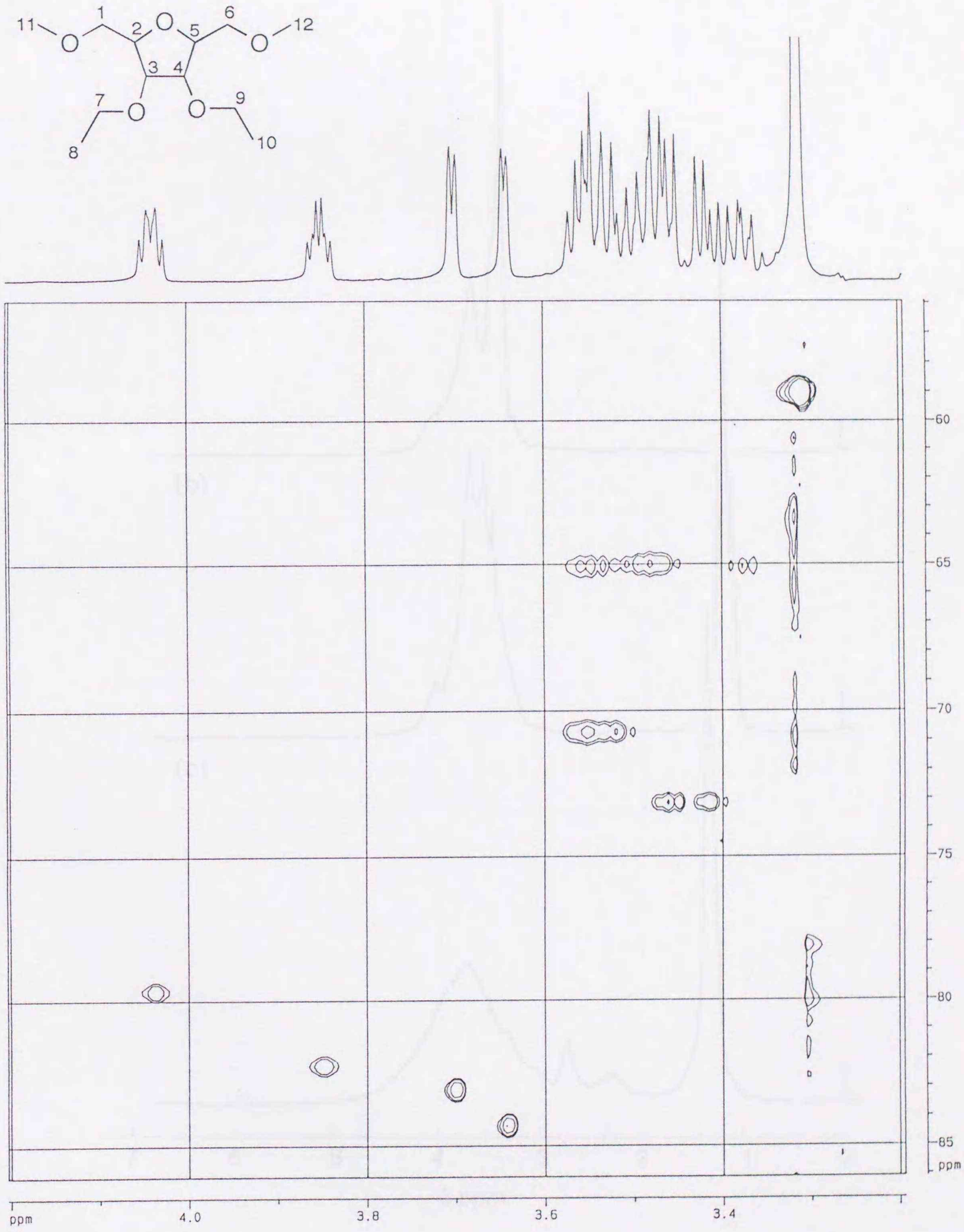


Figure 5.6. Partial HMQC spectrum of 2,5-anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol 77.

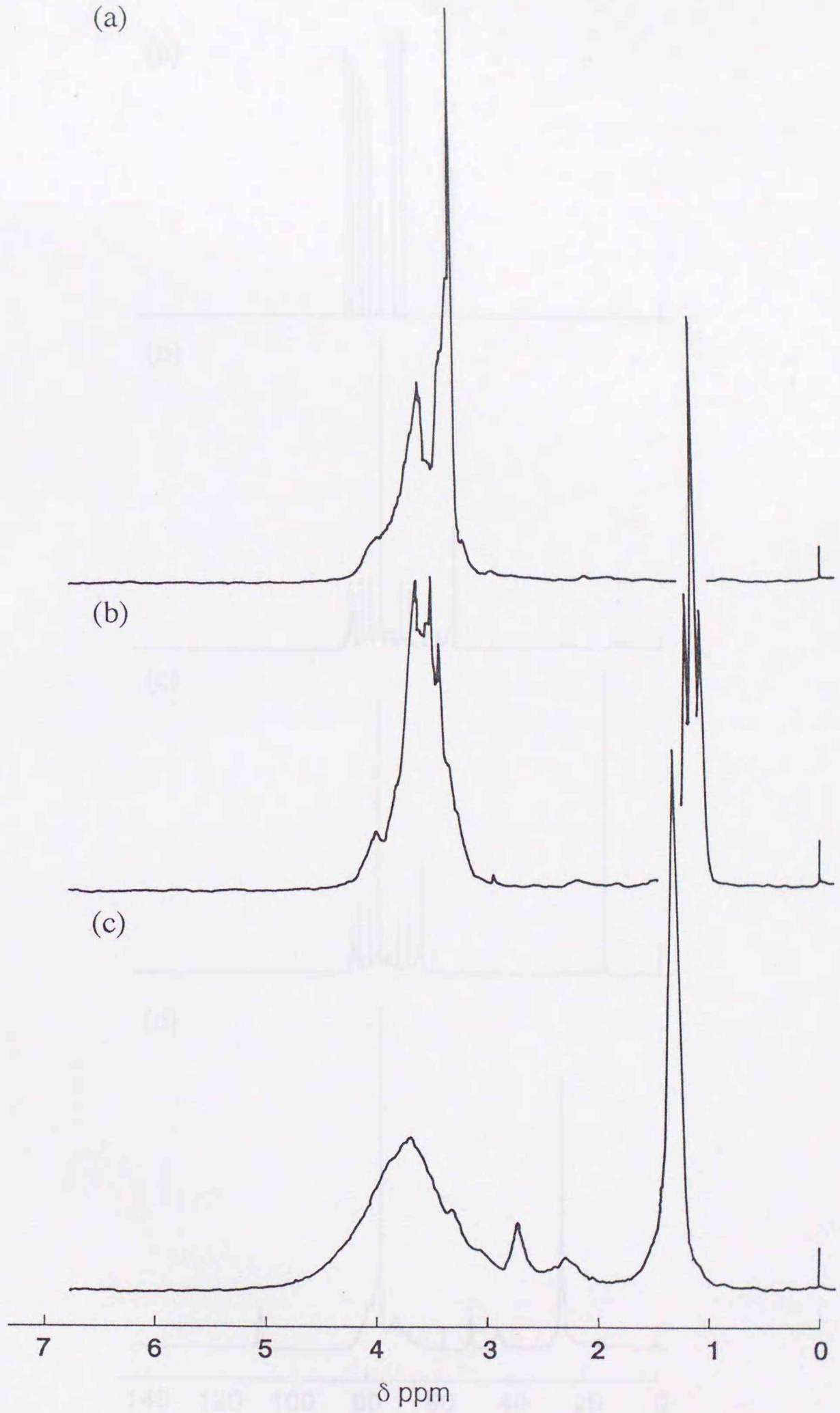


Figure 5.7. ^{1}H NMR spectra of polymers (a) 78, (b) 79, and (c) 80.

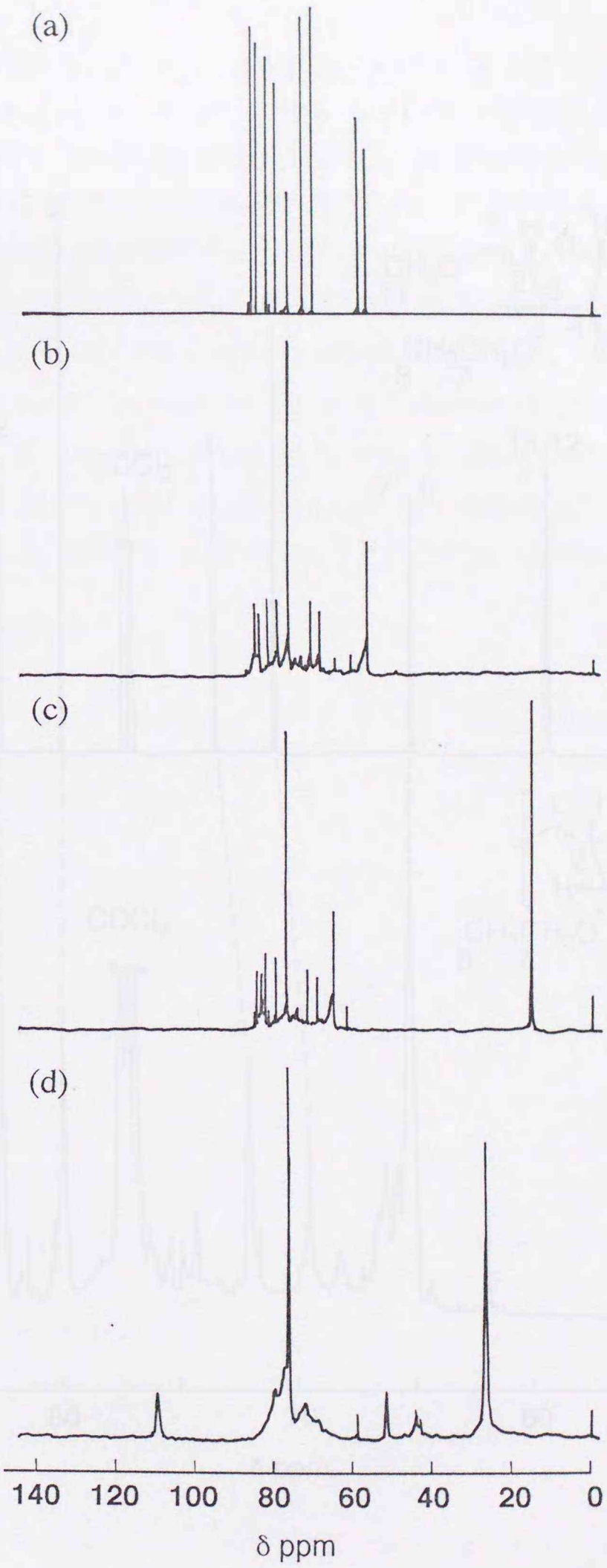


Figure 5.8. ^{13}C NMR spectra of (a) model compound 76, and polymers (b) 78, (c) 79, and (d) 80.

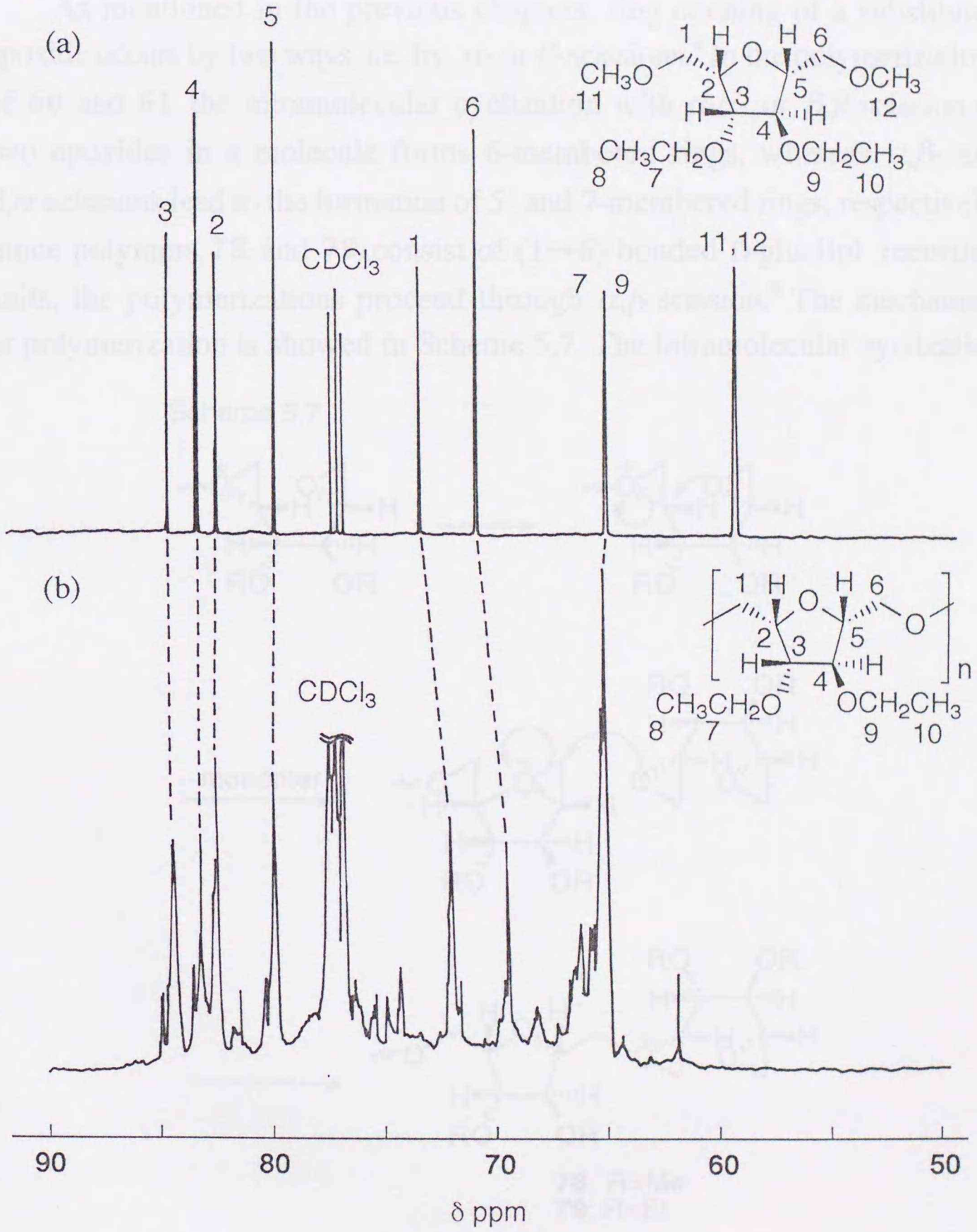
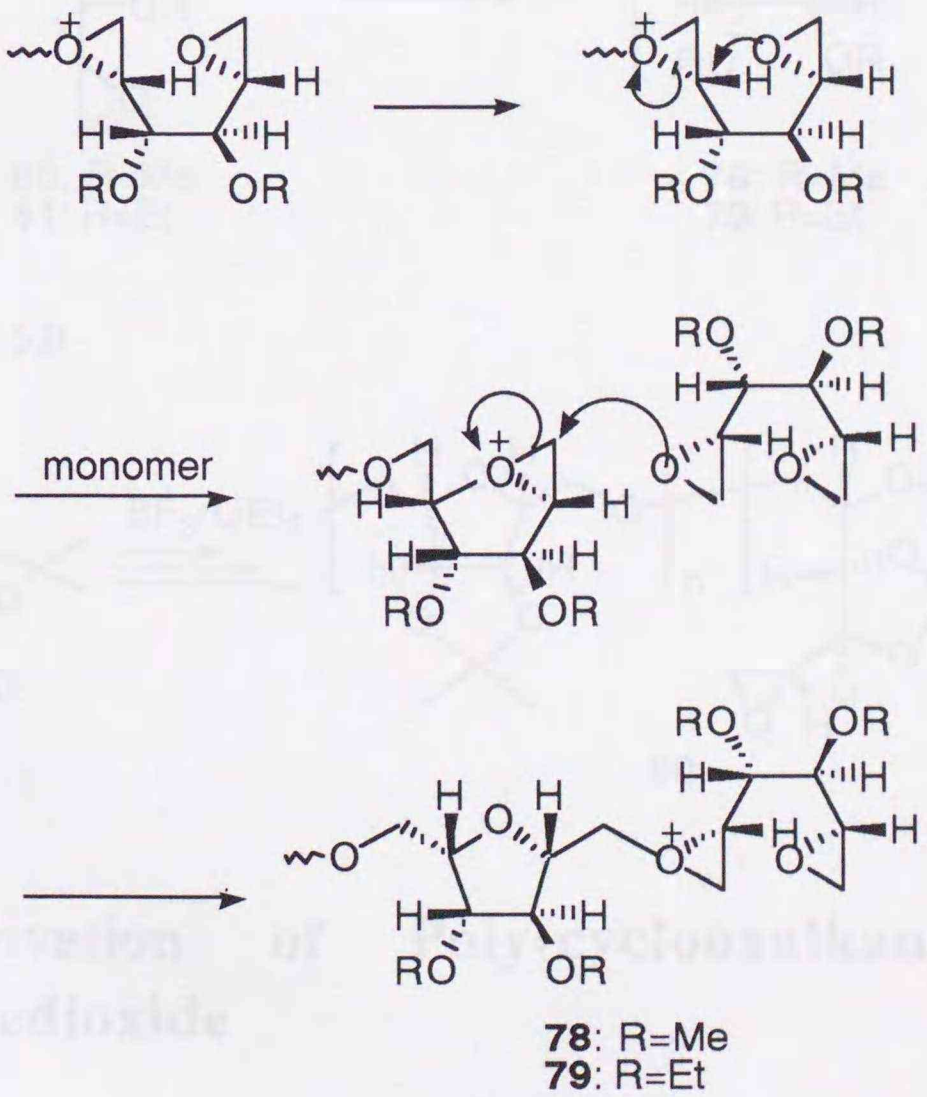


Figure 5.9. Partial ^{13}C NMR spectra of (a) 2,5-anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol 77 and (b) polymer 79.

that the isopropylidene group connected with C-3 and C-4 in D-mannitol precludes the ring closure to make a 5-membered ring. The low cyclopolymerization tendency of **62** is easily understood by this reason.

As mentioned in the previous chapters, ring opening of a substituted epoxide occurs by two ways, i.e. by α- or β-scissions.[8] In the polymerizations of **60** and **61** the intramolecular cyclization with α,α- or β,β-scission of two epoxides in a molecule forms 6-membered rings, whereas α,β- and β,α-scissions lead to the formation of 5- and 7-membered rings, respectively. Since polymers **78** and **79** consist of (1→6) bonded D-glucitol recurring units, the polymerizations proceed through α,β-scission.[9] The mechanism of polymerization is showed in Scheme 5.7. The intramolecular cyclization

Scheme 5.7

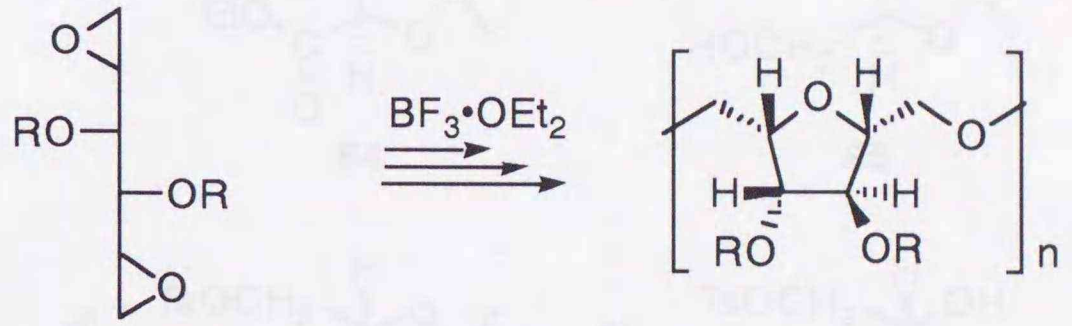


78: R=Me
79: R=Et

occurs the ring opening of the first epoxide with inversion of the configuration via an S_N2[10] attack of the second epoxide function on the α-carbon of the former oxonium ion[11]. The ring opening of the second epoxide takes place at the β-carbon with retention of the configuration,

the carbon at which the attack is stereochemical favorable in the intermolecular propagation. Therefore, poly[(1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol] (polymer **78**) and poly[(1→6)-2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol] (polymer **79**) are yielded by the cyclopolymerizations of **60** and **61**, respectively, as shown in Scheme 5.8. Although polymer **80** contains both cyclic and acyclic recurring units, the cyclic unit consists of (1→6)-2,5-anhydro-3,4-*O*-isopropylidene-D-glucitol in a similar manner as above.

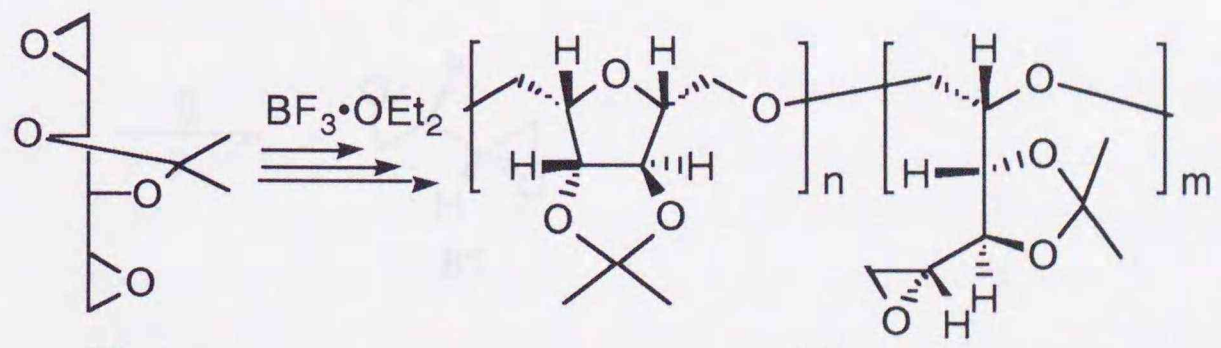
Scheme 5.8



60: R=Me
61: R=Et

78: R=Me
79: R=Et

Scheme 5.9



62

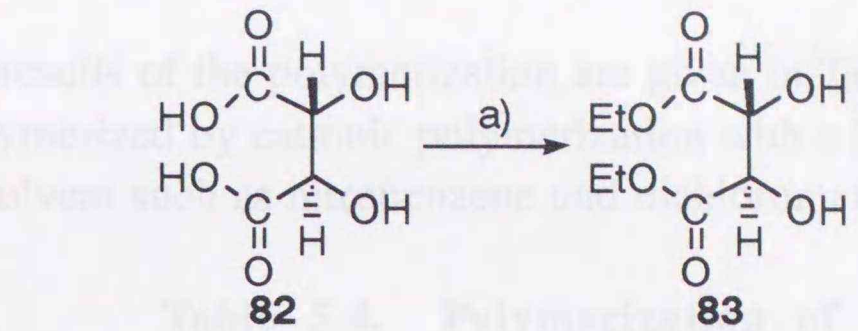
80

5.3 Derivation of Poly(cyclooxalkane) form Butadienedioxide

5.3.1 Preparation of Diepoxide from L-Threitol

In order to develop the synthesis of optically active poly(cyclooxalkane) by the cyclopolymerization of epoxide derived from D-mannitol, L-threitol which has a C_2-axis in analogy with D-mannitol was used as constitutional

Scheme 5.10



a) EtOH / Amberlyst 15 with $CHCl_3$
b) 2,2-Dimethoxypropane / *p*-TsOH in benzene
c) $LiAlH_4$ in ether
d) TsCl in py.
e) 2*N* HCl in MeOH
f) KOH in ether

unit. (*S*,*S*)-1,2:3,4-dianhydro-L-threitol, i.e. (*S*,*S*)-1,2:3,4-butanedioxide **81** was prepared by the method reported by Seebach[13] as indicated in Scheme 5.10.

5.3.2 Polymerization of (*S*,*S*)-1,2:3,4-Butanedioxide

Some results of the polymerization are given in Table 5.4. Diepoxide **81** was polymerized by cationic polymerization with a Lewis acid catalyst in a polar solvent such as nitrobenzene and dichloromethane. The reaction

Table 5.4. Polymerization of (*S*,*S*)-1,2:3,4-butanedioxide (81)[a]

Polymer	Initiator	Solvent	Temp. in °C	Time in h	Yield in %
88	$SnCl_4$	$C_6H_5NO_2$	-25	24	59.8
	CH_2Cl_2		10 min	33.9	
	$BF_3{\bullet}OEt_2$				21.4
89	*t*-BuOK	DMSO	50	1	59.0
				2	95.6[c]

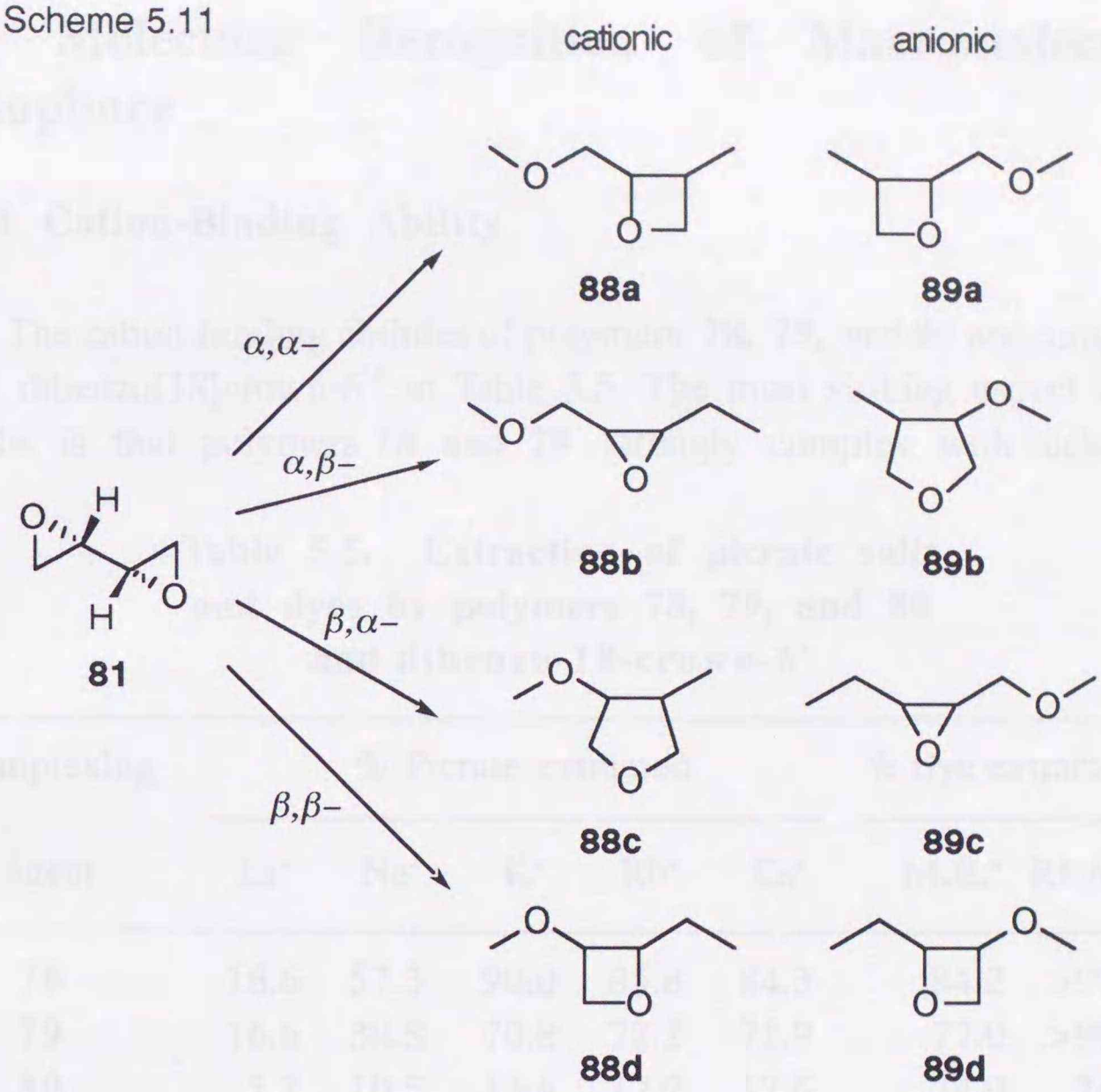
[a] [Monomer]=0.5 mol•L^{-1}; [Initiator]=0.05 mol•L^{-1}.
[b] [Monomer]/[Initiator] monomer ratio=1.
[c] $[\alpha]_D^{20}$ = +33.0°, *c*=7.13 in $CHCl_3$.

system immediately became heterogeneous, when added the catalyst. The polymer obtained was white powder, insoluble in organic solvents. The anionic polymerization with potassium *tert*-butoxide in dimethyl sulfoxide at 50 °C proceeded homogeneously and the polymer obtained was soluble in dimethyl sulfoxide. The polymerization with increasing amount of potassium *tert*-butoxide yielded the polymer which is soluble even in chloroform and benzene. The polymer was optically active with a specific rotation $[\alpha]_D$ of +33° (*c*=7.13 in $CHCl_3$) and its molecular weight measured on vapour pressure osmometer in benzene was 3,300 corresponding to the degree of polymerization of 38.

5.3.3 Structure of Poly[(*S*,*S*)-1,2:3,4-butanedioxide]

In the cationic polymerization of **81**, the intramolecular cyclization with α,α- or β,β-scissions[14] leads to form 4-membered rings (polymers

Scheme 5.11



88a or **88d**), whereas that with α,β- or β,α-scissions to form 3- or 5-membered rings (polymers **88b** or **88c**), respectively (Scheme 5.11). The anionic polymerization occurs the intramolecular cyclization to form 4-membered rings through α,α- or β,β-scissions (polymers **89a** or **89d**) and to form 5- or 3-membered rings through α,β- or β,α-scissions (polymers **89b** or **89c**), respectively. In spite of the diversity of ring formation, there is a strong possibility of 5-membered ring on the basis of thermodynamic stability[15] (polymers **88c** and **89b**). The IR spectra of polymers indicated the absence of epoxy groups showing at 839 and 911 cm^{-1}, and thus, the polymers consist of only cyclic structural units.[16] The ^1H NMR analysis of polymer **89** showed that the cyclic unit is the 5-membered ring having the characteristic proton resonances from 3.5 to 3.7 ppm due to oxymethylene and methine protons.[17]

5.4 Molecular Recognition of Macromolecular Ionophore

5.4.1 Cation-Binding Ability

The cation-binding abilities of polymers **78, 79,** and **80** are compared with dibenzo[18]crown-6[18] in Table 5.5. The most striking aspect in the results is that polymers **78** and **79** strongly complex with such large

Table 5.5. Extraction of picrate salts and dyes by polymers 78, 79, and 80 and dibenzo-18-crown-6[a]

Complexing	% Picrate extracted					% dye extracted	
agent	Li^+	Na^+	K^+	Rb^+	Cs^+	M.B.[b]	Rh.6G[c]
78	18.6	57.3	90.0	85.8	84.3	84.2	>99.9
79	16.6	38.8	70.8	72.2	71.9	77.0	>99.9
80	5.7	10.5	13.6	12.7	12.6	24.9	76.0
DB[18]C-6[d]	3.7	18.3	93.5	84.9	81.6	0.0	0.0

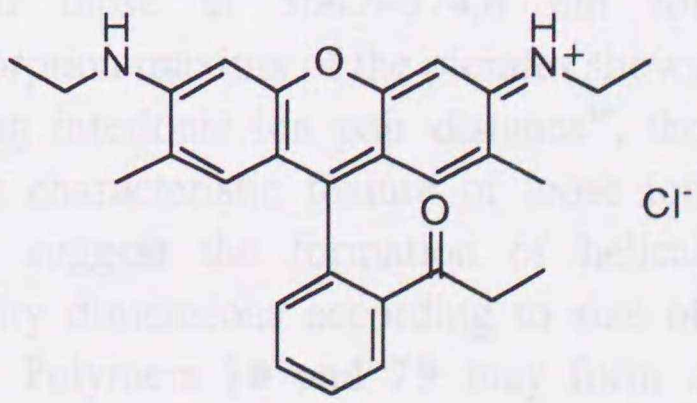
[a] [Polymer]=1 g•L^{-1}; [Picric acid]=7x10^{-5} mol•L^{-1}; [Metal hydroxide]= 0.1 mol•L^{-1}; temp., 23 °C.

[b] [Methylene blue]=2.24x10^{-5} mol•L^{-1}.

[c] [Rhodamine 6G]=2.00x10^{-5} mol•L^{-1}.

[d] [Dibenzo[18]crown-6]=1.26 g•L^{-1} (3.5x10^{-3} mol•L^{-1}).

Methylene blue



Rhodamine 6G

organic cations as rhodamine 6G and methylene blue in addition to alkali metal ions, unlike the crown ether. Polymer **80** showed a lower extractability than polymers **78** and **79**. As the former polymer has a f_c value of 0.5 compared with 1.0 of the latter polymers, the extractability in these polymers is reasonably attributed to the cyclic units, namely, furanose moieties. The characteristics are very similar to those of poly(2,5-tetrahydrofuran)diyl[3] and poly(7-oxanorbornene)[4], which are supposed to form the helical conformers with the flexible binding cavities.

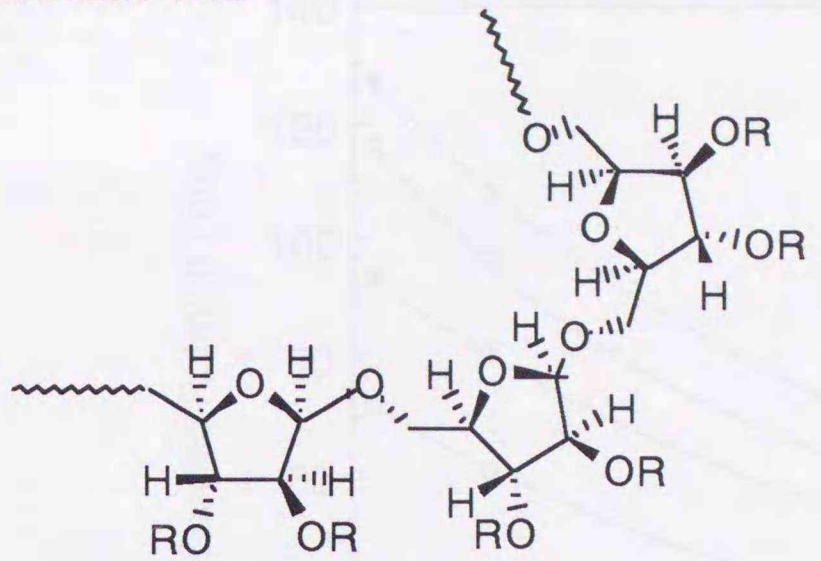
Table 5.6. Absorption maxima of picrate salts in the presence of the complexing agent[a]

Complexing agent	λ_{max} in nm				
	Li^+	Na^+	K^+	Rb^+	Cs^+
78	376.0	376.8	376.0	376.8	376.8
79	377.2	377.2	377.2	377.2	377.2
80	368.8	374.4	374.4	376.0	374.4
Dibenzo[18]crown-6	-	368.0	366.8	368.0	374.8

[a] Solvent, CH_2Cl_2.

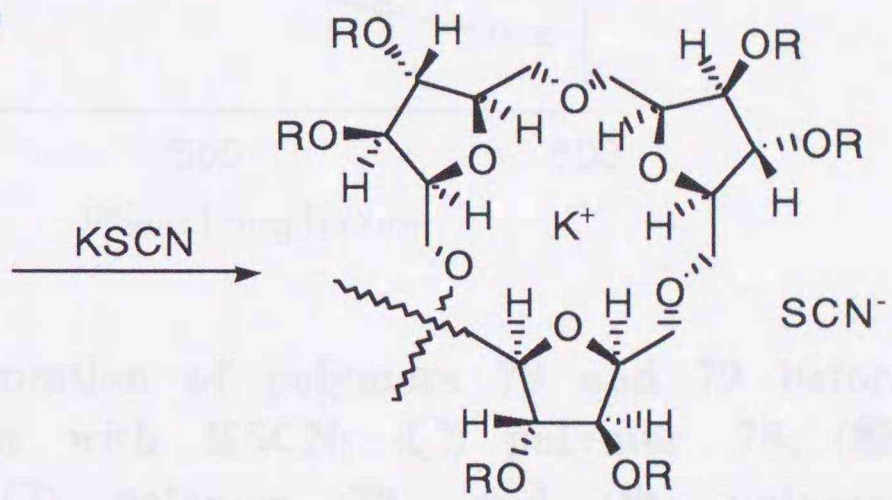
Every complex of the polymers with alkali metal picrates revealed a pronounced bathochromic shift in comparison with the crown complexes as shown in Table 5.6. The absorption maxima for polymers **78**, **79**, and **80**, which are found at 376.0-376.8, 377.2, and 368.8-376.0 nm, respectively, present a contrast to those at 366.8-374.8 nm for dibenzo[18]crown-6. Because the absorption maxima of the picrates shows the bathochromic shift with increasing interionic ion pair distance[19], the complexes of the polymers have the characteristic feature of loose ion pair. These observations, therefore, suggest the formation of helical conformer capable of varying in cavity dimensions according to size of such cations as metal ions and dyes. Polymers **78** and **79** may form a helix consisting of three conformational repeating units in one turn according to Scheme 5.12 shown here. This repeating unit is similar to the cyclic

Scheme 5.12



78: R=Me
79: R=Et

KSCN



90: R=Me
91: R=Et

structure of [18]crown-6. Polymer **80**, however, forms no helix due to the coexistence of acyclic repeating units, and thus, the interionic distance decreases.

The conformational change of helical structure reflected in specific rotation and CD profile. The complexes of polymers **78** and **79** with potassium thiocyanate changed in specific rotation in comparison with the original polymers as shown in Figure 5.10. An increase in specific rotation should be attributed to the formation of helical structure. The CD spectra of polymer **79** indicated no change in the ultraviolet region by the addition of potassium thiocyanate, but recognized a slight shift from 170 to 171.5 nm on the measurement in hexafluoroisopropanol.

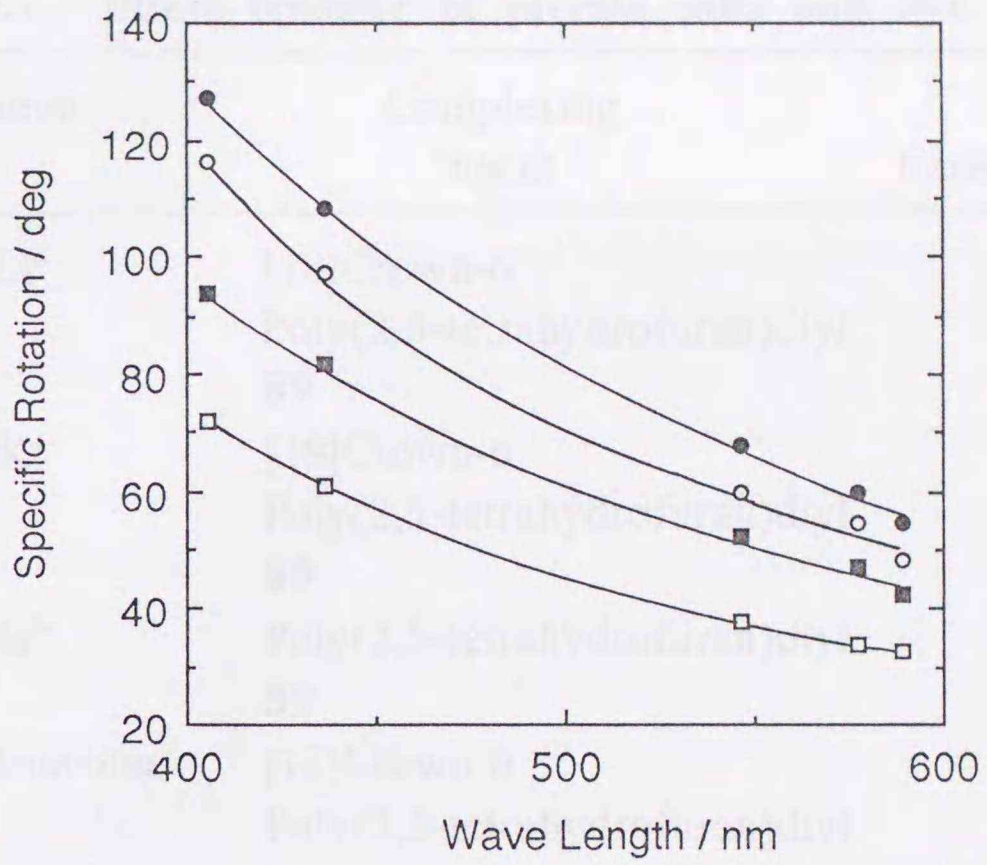


Figure 5.10. Specific rotation of polymers 78 and 79 before and after complexation with KSCN: (○) polymer 78, (●) polymer 78•KSCN, (□) polymer 79, and (■) polymer 79•KSCN.

The ^{1}H NMR spectrum of polymer **78** in the presence of potassium thiocyanate showed the broadening of the signals, thus recognizing the complex formation and presumably supporting the fixed helical structure.[20] The ^{13}C NMR spectrum of the complex had a carbon signal due to thiocyanate at 131.9 ppm.

Polymer **89** prepared with potassium *tert*-butoxide catalyst in dimethyl sulfoxide, was used for extraction of cations. Table 5.7 compares the cation-binding ability of the polymer with [18]crown-6 and poly(2,5-tetrahydrofuran)diyl. Polymer **89** is more effective in binding larger cations like methylene blue, but less effective for smaller cations like Li^{+}, K^{+}, and Ba^{2+}. The cavity of helical turn well suited to the size of methylene blue (Scheme 5.13).

Table 5.7. Phase transfer of picrate salts and dye extractions[a]

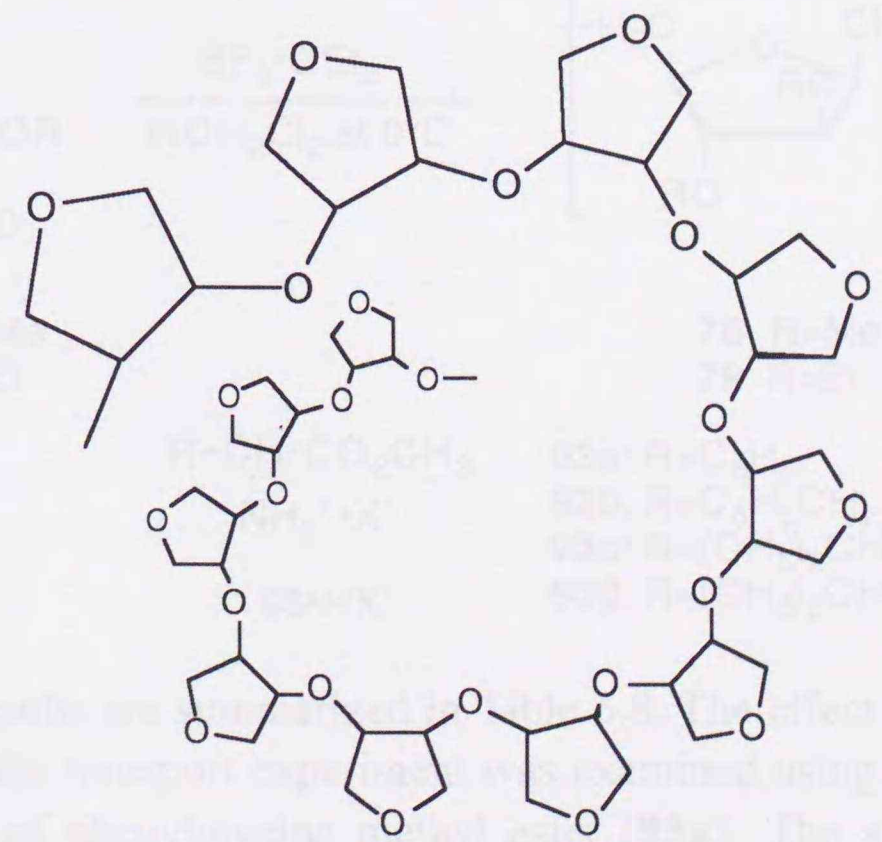
Cation	Complexing agent	Salt transferred (%)
Li^+	[18]Crown-6	63[b]
	Poly(2,5-tetrahydrofuran)diyl	37[b]
	89	0
K^+	[18]Crown-6	74[b]
	Poly(2,5-tetrahydrofuran)diyl	53[b]
	89	1
Ba^{2+}	Poly(2,5-tetrahydrofuran)diyl	67[b]
	89	0
Methylene blue[c]	[18]Crown-6	2[b]
	Poly(2,5-tetrahydrofuran)diyl	83[b]
	89	80

[a] [Salt]=0.025 g•L^{-1} in water; [complexing agent]=2.5 g•L^{-1} in $CHCl_3$ at 25 °C.

[b] Ref.4.

[c] Dye extractions were performed by using equal solution volumes of methylene blue (0.1 mg in water) and complexing agent (140 mg in chloroform).

Scheme 5.13



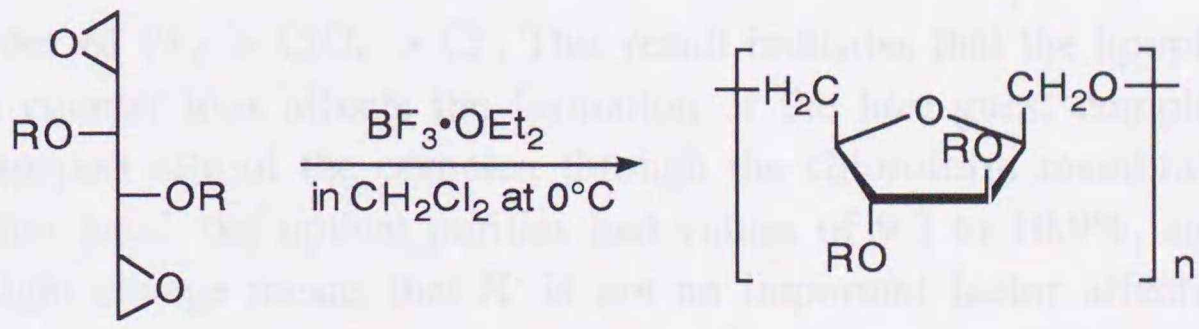
92

5.4.2 Enantioselective Membrane Transport of Racemic Amino Acid

These polymers **78** and **79** are supposed to form helical conformers capable of varying pitch and cavity size to optimize multidentate coordination with a given cation. This host-guest complexation mechanism is similar to that for naturally occurring acyclic ionophores which accommodate guest metal cations in their pseudo-cyclic cavities and transport a guest across the biomembrane. These polymers, therefore, are a new class of host polymers, namely, a macromolecular ionophore. Host polymers **78** and **79** consist of chiral constitutional repeating units, whose asymmetric character is distinct from the other macromolecular ionophores. Of greater interest, therefore, is the observation of the chiral recognition property of host polymers **78** and **79** toward a racemic guest.

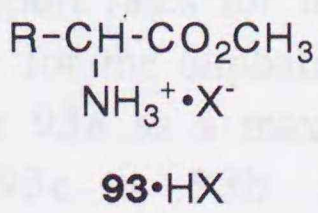
The enantioselective transport of racemic methyl amino esters **93** was achieved using a system involving aqueous providing and receiving phases separated by a chloroform phase containing poly[(1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol] (polymer **78**).

Scheme 5.14



60: R=Me
61: R=Et

78: R=Me
79: R=Et



93•HX

93a: R=C_6H_5
93b: R=$C_6H_5CH_2$
93c: R=$(CH_3)_2CH$
93d: R=$(CH_3)_2CHCH_2$

Typical results are summarized in Table 5.8. The effect of the counter anion (X^-) on the transport experiment was examined using HPF_6, $HClO_4$, and HCl salts of phenylglycine methyl ester (**93a**). The amount of **93a** transported to the receiving phase was 31.5% for PF_6^- and decreased in

Table 5.8. Enantioselective transport of DL-$RCH(CO_2CH_3)NH_3^+ \cdot X^-$ (93•HX) by poly[(1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol] (78)

		Guest in receiving phase (β-arm)		
93 (R)	X^-	Transported %[a]	Optical purity %[b]	Faster moving enantiomer
93a (C_6H_5)	PF_6^-	31.5	10.9	L
	ClO_4^-	9.4	10.7	L
	Cl^-	2.1	9.3	L
93b ($C_6H_5CH_2$)	PF_6^-	30.9	2.3	L
93c ($(CH_3)_2CH$)	PF_6^-	17.8	7.3	L
93d ($(CH_3)_2CHCH_2$)	PF_6^-	16.7	2.3	L

[a] Transported after 120 h.

[b] Analyzed by HPLC when the 30% of guest was transported from source phase to receiving phase.

the order of $PF_6^- > ClO_4^- > Cl^-$. This result indicates that the lipophilicity of the counter ions affects the formation of the host-guest complex and the transport rate of the complex through the chloroform membrane. On the other hand, the optical purities had values of 9.3 to 10.9%, and thus this slight change means that X^- is not an important factor affecting the chiral recognition property of polymer **78**. The structural effect of a guest on transport was elucidated using HPF_6 salts of methyl amino esters (**93**•HPF_6^-). The transport rates for the aromatic guests, **93a** and **93b**, were faster than those for the aliphatic ones, **93c** and **93d**. The optical purity was 10.9% for **93a** as a maximum value and decreased in the order of **93a** > **93c** > **93b** > **93d**, which conforms to the character of the R group of $RCH(CO_2CH_3)NH_3^+ \cdot PF_6^-$ in the following sense: the greater the steric requirements of this group in the vicinity of the chiral center of the guest, the higher the chiral recognition. The characteristic of the chiral recognition of polymer **78** is very similar to that of the chiral crown ethers incorporating 1,1'-binaphthyl units reported

by Cram et al.[21] For all the host-guest systems, the faster moving enantiomer was the L-form.

The formation of a host-guest complex was observed by NMR spectral measurements, when the transport experiment was carried out in $CDCl_3$ under the same condition as described in Table 5.8. Figure 5.11 shows the ^{13}C NMR spectra of polymer **78** before and after the complexation with D- or L-**93a**•PF_6^-. The absorptions at 84.7, 85.4, and 69.3 ppm due to the C-3, C-4, and C-6 carbons in 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units were singlet before the host-guest complexation. On the other hand, the absorptions at the C-3, C-4, and C-6 split into multiplets after the complex formation between polymer **78** and D-**93a**•PF_6^-, and those at C-4 and C-6 after the complexation of polymer **78** and L-one. This result indicates that the oxygens attached to the C-3, C-4, and C-6 carbons act as a donor atom for the host-guest complexation. Figure 5.12 shows the ^1H NMR spectra of guests for the transport experiments using D-, L-, or DL-**93a**•PF_6^-. The broad absorptions at 7.36 and 7.42 ppm due to the ortho protons (H_1) were observed for the transport system using DL-**93a**•PF_6^-. The former (H_{1L}) and the latter (H_{1D}) agreed with the absorption for L-**93a** and for D-**93a** in the host-guest complexation, respectively. The H_{1L}/H_{1D} areal ratio was 1.35, a value which is close to the L-**93a** / D-**93a** ratio of 1.25 (optical purity, 10.9%) in Table 5.8. These results indicate that the coordination environments of polymer **78** with L-**93a** differ from that of D-**93a**, and the polymer **78**-L-**93a** complex is more stable than the polymer **78**-D-**93a** one. Consequently, this difference in stability causes the predominant transport of the L-isomer to polymer **78**.

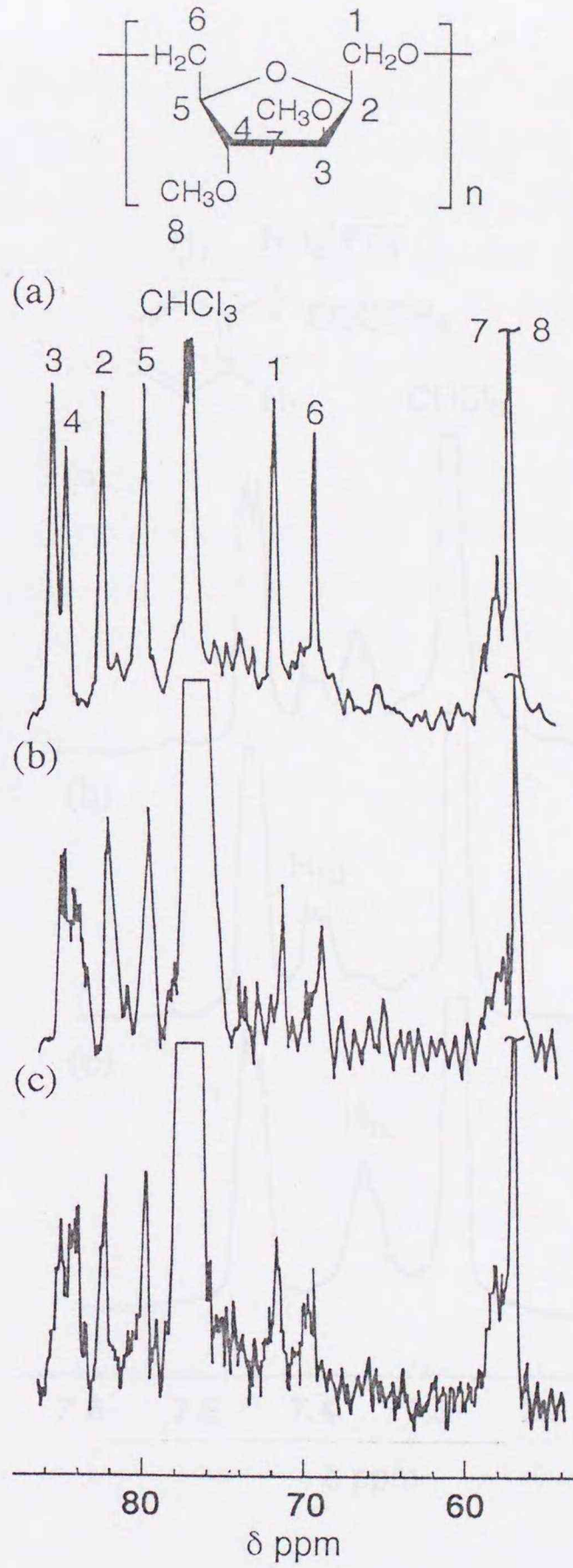


Figure 5.11. ^{13}C NMR spectra of polymer 78 before (a) and after the complexation with D- or L-93a•PF_6^-: (b) polymer 78 / D-isomer; (c) polymer 78 / L-isomer.

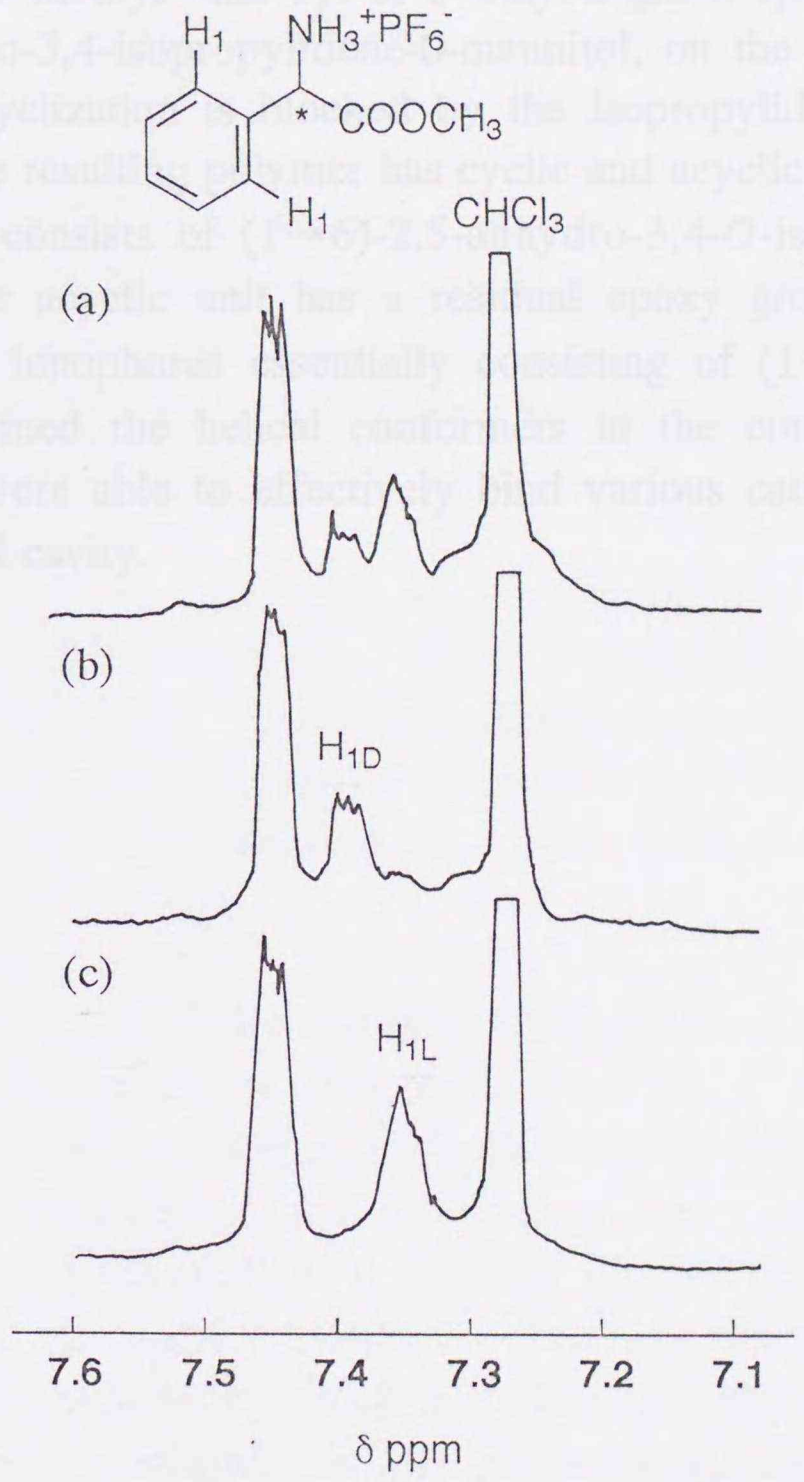


Figure 5.12. ^{1}H NMR spectra of the aromatic protons of 93a for the transport experiments of DL-, D-, or L-93a•PF_6^- using polymer 78: (a) DL-, (b) D-, and (c) L-93a•PF_6^-.

5.5 Conclusion

The cyclopolymerization of diepoxides, namely, 1,2:5,6-dianhydro-3,4-di-*O*-methyl- and 3,4-di-*O*-ethyl-D-mannitol, give poly[(1→6)-2,5-anhydro-3,4-di-*O*-methyl- and 3,4-di-*O*-ethyl-D-glucitol]s. In the case of 1,2:5,6-dianhydro-3,4-isopropylidene-D-mannitol, on the other hand, the intramolecular cyclization is blocked by the isopropylidene group, and consequently, the resulting polymer has cyclic and acyclic repeating units. The cyclic unit consists of (1→6)-2,5-anhydro-3,4-*O*-isopropylidene-D-glucitol, and the acyclic unit has a residual epoxy group as pendant. Macromolecular ionophores essentially consisting of (1→6) bonded D-glucitol unit formed the helical conformers in the complexation with cations, which were able to effectively bind various cations by varying size in the helical cavity.

5.6 Experimental Section

Measurements. NMR spectra were recorded on a Hitachi R90H, a Bruker MSL-400, or a Bruker AMX-600 spectrometer. DEPT, COSY, HMQC, HMBC, DQF-COSY, and NOESY techniques were utilized for assignment of NMR spectra of model compounds and polymers. IR spectra were measured on a Jasco A-102 spectrometer. Circular dichroism (CD) spectra were recorded on a Jasco J-720 spectropolarimeter in hexafluoroisopropanol and specific rotations were measured with a Jasco DIP-140 digital polarimeter. UV spectra were recorded on a Jasco UVIDEC-660 spectrometer. Gel permeation chromatography (GPC) in tetrahydrofuran was performed on a WATERS M45 high performance liquid chromatograph equipped with three columns (Shodex KF-804F).

Materials. Solvents for synthesis and polymerization were dried by general methods: dichloromethane, 1,2-dichloroethane, and nitroethane were dried over CaH_2 and toluene was distilled from sodium-benzophenone. Dibenzo[18]crown-6 was prepared by the method of Pedersen.[22] Methylene blue, rhodamine 6G, and potassium thiocyanate were used a commercial reagent.

1,2:5,6-Di-*O*-isopropylidene-D-mannitol (64)[23]. A mixture of 272.6 g (2.0 mol) of anhydrous zinc chloride in 1400 mL of dry acetone was shaken vigorously and was filtered into a three-necked 2 L round-bottomed flask, equipped with a drying tube, a condenser, and a mechanical stirrer, containing 141.9 g (0.78 mol) of D-mannitol **63**, and the suspension was stirred vigorously for about 3 h until **63** dissolved at room temperature. The solution was poured into a beaker containing a solution of 343 g of potassium carbonate in 343 mL of water. The suspension was mechanically stirred until the evolution of gases slackened. The mixture was filtered through a Büchner funnel, leaving a white precipitate. The filtrate was evaporated under reduced pressure, and the residue was extracted with chloroform. The precipitate was washed three times with chloroform, and the suspension was filtered each time. The combined extracts were dried with anhydrous sodium sulfate, and evaporated to dryness, giving 78.4 g (38%) of colourless crystals. The product was dissolved in 78.4

mL of chloroform and 784 mL of hexane under reflux. The hot solution was filtered, and to the filtrate 784 mL of hexane was added, and kept overnight in refrigerator to give 98.1 g (48%) of colourless crystals of **64**, mp 126.2-127.0 °C, IR (KBr) 3280 (OH), 2995, 2940, 2895 (CH), 1387, 1376 (CCH_3), 1160, 1126, and 1044 cm^{-1} (1,3-dioxolane ring).

1,2:5,6-Di-*O*-isopropylidene-3,4-di-*O*-methyl-D-mannitol (65)[5]. A mixture of 42.1 g (0.16 mol) of **64** and 200 mL of dimethyl sulfoxide was placed in 500 mL of a three-necked round-bottom flask equipped with a mechanical stirrer, a condenser, and a dropping funnel. To the solution a mixture of 32.3 g (0.81 mol, 5 equiv) of sodium hydroxide and 32.3 mL of water was added all at once, and 51.2 g (0.40 mol, 2.5 equiv) of dimethyl sulfate was added dropwise through the addition funnel at such a rate that the temperature of the reaction mixture did not exceed 60 °C. The reaction mixture was heated at 60 °C with water bath, and followed by stirring overnight at room temperature. The content of the flask was then poured into a beaker containing 250 mL of water, and extracted with chloroform (3 x 100 mL). The combined organic layer washed with water and dried with anhydrous sodium sulfate. The chloroform which was evaporated under reduced pressure, gave a syrup that was distilled under vacuum to give 42.2 g (90.7%) of a colourless liquid **65**, bp 119.5-120.7 °C / 0.65 mmHg. IR (film): 2960, 2910, 2860, 2805 (C-H), 1370, 1360 (CCH_3), 1085 cm^{-1} (C-O-C). ^1H NMR ($CDCl_3$) δ 3.94-4.23 (m, -OCH- and $-OCH_2-$, 8H), 3.50 (s, $-OCH_3$, 6H), 1.41 (s, CCH_3, 6H) and 1.36 ppm (s, CCH_3, 6H).

1,2:5,6-Di-*O*-isopropylidene-3,4-di-*O*-ethyl-D-mannitol (66)[5]. A solution of 20 g (76.2 mmol) of **64** in 60 mL of dimethyl sulfoxide was treated with a solution of 60 g (1.5 mol) of sodium hydroxide in 60 mL of water and 112.5 g (730 mmol) of diethyl sulfate as described for **65**, to give, after distillation, 21.6 g (89%) of **66**, bp 106.0-109.8 °C / 0.3 mmHg. ^1H NMR ($CDCl_3$) δ 4.23-3.93 (m, -OCH- and $-OCH_2-$, 8H), 3.65 (q, $\underline{CH_2}CH_3$, 4H), 1.40 (s, CCH_3, 6H), 1.34 (s, CCH_3, 6H), and 1.18 ppm (t, $CH_2\underline{CH_3}$, 6H).

3,4-Di-*O*-methyl-D-mannitol (67)[5]. A mixture of 42.2 g (0.15 mol) of **65**, 120 mL of acetic acid, and 60 mL of water was placed in 300 mL of round-bottom flask and heated at 100 °C for 30 min. After cooling to room temperature, the acetic acid and water were evaporated under reduced pressure. The residue was diluted with 100 mL of water and evaporated. Then into the flask 100 mL of ethanol was added and evaporated. The residue was recrystallized from ethanol, to give 26.1 g (86%) of **67**.

3,4-Di-*O*-ethyl-D-mannitol (68)[5]. 21.6 g (67.9 mmol) of **66** was hydrolyzed by the procedure similar to that for **67** to give 11.3 g (70%) of **68**.

2,5-Di-*O*-acetyl-3,4-di-*O*-methyl-1,6-di-*O*-(methylsulonyl)-D-mannitol (69)[5]. To a stirred solution of 26.0 g (123.7 mmol) of **67** in 370 mL of dry pyridine was added dropwise 31.1 g (271.1 mmol, 2.2 equiv) of methanesulfonyl chloride during 1 h at -10 °C. The reaction mixture was then removed from the cooling bath and was kept for 30 min at 0 °C, and for 30 min at room temperature. The mixture was then cooled to -10 °C, and 40.0 g (391.8 mmol, 3.2 equiv) of acetic anhydride was added dropwise and the solution was kept overnight at 0 °C. The contents of flask was poured into a water and was extracted with chloroform. The organic layer was dried with sodium sulfate, and evaporated. To the residue was added toluene and then evaporated, to yield 50.9 g (91.3%) of a syrup that was used in next step without further purification. ^{1}H NMR ($CDCl_3$) δ 3.48 (s, OCH_3, 6H), 3.05 (s, SO_2CH_3, 6H), and 2.15 ppm (s, $COCH_3$, 6H).

2,5- Di- *O*- acetyl- 3,4- di- *O*- ethyl- 1,6-di-*O*-(methylsulonyl)-D-mannitol (70)[5]. The solution of 11.3 g (47.3 mmol) of **66** in 142 mL of dry pyridine was treated with 11.9 g (104.1 mmol, 2.2 equiv) of methanesulfonyl chloride and 15.4 g (150.8 mmol, 3.2 equiv) of acetic anhydride as described for **69**, to give 21.6 g (95%) of **70**.

1,2:3,4:5,6-Tri-*O*-isopropylidene-D-mannitol (71)[24]. To a suspension of 125 g (686 mmol) of **63** and 1560 mL of acetone in 2 L of two-necked round-bottom flask was added 12.5 mL of 97% of sulfuric

acid and the solution was stirred with a mechanical stirrer at room temperature for 29 h. The mixture was neutralized with 58 mL of 25% of an aqueous solution of NH_4OH and 78 g of sodium carbonate. The mixture was filtered and the filtrate was evaporated to give a solid, which was recrystallized from the ethanol to give 129.6 g (62.5%) of a white needle crystal, mp 69.5-72.3 °C. $[\alpha]_D$ +14.2° (*c*=1.0, in CH_2Cl_2 at 20.0 °C).

3,4-*O*-Isopropylidene-D-mannitol (72)[24]. In a 2 L of round-bottom flask a mixture of 119.4 g (395 mmol) of **71** and 2 L of 70% acetic acid was heated at 40 °C with magnetically stirring for 1.5 h. The acetic acid was evaporated under vacuum and 1 L of acetone was added. An insoluble part was filtered off and the acetone was removed under vacuum. The residue was recrystallized from 1 L of acetone to give 69.9 g (79.6%) of a white crystal, mp 86.5-87.5 °C.

3,4-*O*-Isopropylidene-1,6-di-*O*-tosyl-D-mannitol (73)[24]. In a 1 L of four-necked round-bottom flask placed 34.9 g (157.2 mmol) of **72** and 500 mL of pyridine, the mixture was cooled to -5 °C and 61.3 g (321.3 mmol, 2 equiv) of tosyl chloride was added under stirring for 4 h at 0 °C. The flask content was pound into a mixture of 1 L of 6*N* HCl and 470 mL of ether which was cooled with ice-water bath. The mixture was transferred into a separated funnel and the organic layer was separated. The aqueous layer was extracted with ether and the combined ether was washed with 3% of an aqueous solution of $NaHCO_3$, dried with sodium sulfate, and evaporated to give a 73.9 g (88.6%) of syrup that was used without further purifications.

1,2:5,6-Dianhydro-3,4-di-*O*-methyl-D-mannitol (60)[5]. The solution of 50.9 g (113 mmol) of **69** in 170 mL of dry chloroform was placed in 300 mL of round-bottom flask, and then was treated with 51 mL of the solution of 4.3 M of methanolic sodium methoxide at 10 °C for 1 h. The flask content was poured into water, and was extracted with chloroform. The extract was dried with sodium sulfate and the chloroform was removed under vacuum. The residue was distilled under vacuum, to yield 8.6 g (44%) of a colourless liquid, bp 69.9-71.8 °C / 0.5 mmHg.

The specific rotation of **60** in $CHCl_3$ (c 0.14) at 22 °C: $[\alpha]_D$ -7.32°, $[\alpha]_{577}$ -7.96°, $[\alpha]_{546}$ -9.17°, and $[\alpha]_{435}$ -15.04°. IR (film) 2980, 2925, 2890, 2820 (C-H), 1091 (C-O-C), 938, 847, 835 cm^{-1} (epoxy). ^1H NMR ($CDCl_3$) δ 3.48 (s, OCH_3, 6H), 3.4-2.75 ppm (m, -OCH- and epoxy, 8H). *Anal.* Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 54.38; H, 8.03.

1,2:5,6-Dianhydro-3,4-di-*O*-ethyl-D-mannitol (61)[5]. The solution of 22.6 g (47.3 mmol) of **70** in 72 mL of dry chloroform was treated with 24.2 mL of the solution of 4.3 M of methanolic sodium methoxide at 10 °C for 1 h, to yield 5.1 g (22%) of a colourless liquid, bp 75.2-76.1 °C / 0.25 mmHg. The specific rotation of **61** in $CHCl_3$ (c 1.30) at 22 °C: $[\alpha]_D$ -5.18°, $[\alpha]_{577}$ -4.72°, $[\alpha]_{546}$ -5.20°, $[\alpha]_{435}$ -7.22°, and $[\alpha]_{405}$ -7.79°. IR (film) 2975, 2930, 2875 (C-H), 1092 (C-O-C), 846, 819 cm^{-1} (epoxy). ^1H NMR ($CDCl_3$) δ 3.84-3.46 (m, -OCH- and -O$\underline{CH_2}CH_3$, 6H), 3.31-3.11 and 2.91-2.76 (m epoxy 6H), 1.203 (t, $CH_2\underline{CH_3}$, 6H). *Anal.* Calcd for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 58.29; H, 9.00.

1,2:5,6-Dianhydro-3,4-*O*-isopropylidene-D-mannitol (62)[24]. A mixture of 73.9 g (139.3 mmol) of tosylate **73**, 96.3 g (696.5 mmol, 5 equiv) of anhydrous potassium carbonate, and 860 mL of methanol in 1 L round-bottom flask was heated at 25 °C with a vigorous stirring for 2.5 h. Into the mixture 900 mL of water was added to dissolve potassium carbonate. The solution was extracted with dichloromethane (200 mL x 4) and the combined organic layer was washed with 3% of an aqueous solution of ammonium chloride (250 mL x 2), dried with anhydrous sodium sulfate, and then the dichloromethane was evaporated. The residue was distilled under vacuum to give 15.1 g (57.1%) of a colourless liquid, bp 89.1-90.5 °C / 0.5 mmHg. IR (film) 2990 (ν, C-H), 1059 (C-O-C), 860 cm^{-1} (epoxy). ^1H NMR ($CDCl_3$) δ 3.83 (dd, *J*=3.08, 1.32, -OCH-, 2H), 3.18-3.05 (m, epoxy methine, 2H), 2.84 (dd, *J*=4.07, 4.94, epoxy methylene, 2H), 2.71 (dd, *J*=2.64, 4.84, 2H), and 1.44 ppm (s, CCH_3, 6H). *Anal.* Calcd for $C_9H_{14}O_4$: C, 58.04; H, 7.58. Found: C, 58.02; H, 7.65.

2,5-Anhydro-3,4-di-*O*-methyl-D-glucitol (74). The mixture of 1.75 g (10 mmol) of **60**[5] and 40 mL of water was heated under reflux for 7 h and the solution was then evaporated under reduced pressure to obtain a syrup from which the waters were removed by azeotropic distillation with benzene and chloroform two times. The mixture was separated by a flush column chromatography, using ethyl acetate / isopropanol (5 / 1). The fractions having R_f 0.5 gave, on evaporation, 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol as a syrup (1.60 g, 82%). The specific rotation of **74** in $CHCl_3$ (c 1.11) at 20 °C: $[\alpha]_D$ +64.1°, $[\alpha]_{577}$ +66.1°, $[\alpha]_{546}$ +74.8°, $[\alpha]_{435}$ +125.0°, and $[\alpha]_{405}$ +149.6°. IR (film): 3370 (OH), 2920, 2870, 2810 (ν, C-H), 1085 cm^{-1} (ν_{as}, C-O-C). ^{13}C NMR ($CDCl_3$) δ 86.17 (C-3), 84.44 (C-5), 83.60 (C-4), 80.38 (C-2), 62.85 (C-6), 61.47 (C-1), 10.30, 10.35 ppm (CH_3-). *Anal.* Calcd for $C_8H_{16}O_5$: C, 49.99; H, 8.39. Found: C, 49.22; H, 8.44.

2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol (76). To a stirred solution of 0.96 g (5 mmol) of **74** in 6.4 mL of dimethyl sulfoxide were simultaneously added a solution of 1 g of sodium hydroxide in 1 mL of water and 1.60 g (12.6 mmol) of dimethyl sulfate at the temperature being kept below 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, evaporated, and the residue was separated by a column chromatography, using ether / *n*-hexane (1 / 1). The fractions having R_f 0.45 gave, on evaporation, **76** as a colourless liquid (0.55 g, 50%). The specific rotation of **76** in $CHCl_3$ (c 1.058) at 20 °C: $[\alpha]_D$ +66.7°, $[\alpha]_{577}$ +69.8°, $[\alpha]_{546}$ +78.6°, $[\alpha]_{435}$ +130.1°, and $[\alpha]_{405}$ +155.4°. IR (film): 2975, 2900, 2890, 2810 (ν, C-H), 1100 cm^{-1} (ν_{as}, C-O-C). ^1H NMR (400 MHz, $CDCl_3$) δ 4.09 (H-5, $^3J_{H\text{-}6A,H\text{-}5}$=6.8Hz, $^3J_{H\text{-}6B,H\text{-}5}$=5.0Hz, $^3J_{H\text{-}5,H\text{-}4}$=4.3Hz), 3.92 (H-2, $^3J_{H\text{-}2,H\text{-}1A}$=5.9Hz, $^3J_{H\text{-}2,H\text{-}1B}$=5.9Hz, $^3J_{H\text{-}2,H\text{-}3}$=3.6Hz), 3.68 (H-4, $^3J_{H\text{-}4,H\text{-}5}$=4.1Hz, $^3J_{H\text{-}4,H\text{-}3}$=0.8Hz), 3.64 (H-3, $^3J_{H\text{-}3,H\text{-}2}$=3.9Hz, $^3J_{H\text{-}3,H\text{-}4}$=1.2Hz), 3.64 (A) and 3.59 (B) (H-6, $^3J_{H\text{-}6A,H\text{-}5}$=6.8Hz, $^3J_{H\text{-}6B,H\text{-}5}$=5.0Hz, $^3J_{H\text{-}6A,H\text{-}6B}$=10.2Hz), 3.55 (A) and 3.47 (B) (H-1, $^3J_{H\text{-}1A,H\text{-}2}$=6.0Hz, $^3J_{H\text{-}1B,H\text{-}2}$=5.9Hz, $^3J_{H\text{-}1A,H\text{-}1B}$=10.0Hz), 3.40 ($\underline{CH_3}$O-C1), 3.40 ($\underline{CH_3}$O-C6), 3.39 ($\underline{CH_3}$O-C4), 3.38 ppm ($\underline{CH_3}$O-C3). ^{13}C NMR ($CDCl_3$) δ 85.69, 84.75, 82.26, 79.83, 73.15, 70.66, 59.25, 59.19,

57.42, 57.35 ppm. *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-D-glucitol (75). A mixture of 0.52 g (2.6 mmol) of **61**[5] and 10 mL of water was treated as described for **74**, to give pure **75** (0.35 g, 67%) after column chromatography, using chloroform / isopropanol (8 / 2, R_f 0.76). The specific rotation of **75** in $CHCl_3$ (c 1.09) at 20 °C: $[\alpha]_D$ +61.0°, $[\alpha]_{577}$ +64.2°, $[\alpha]_{546}$ +71.9°, $[\alpha]_{435}$ +117.8°, and $[\alpha]_{405}$ +139.4°. IR (film) 3390 (OH), 2960, 2930, 2870 (ν, C-H), 1100, 1065, and 1040 (ν, C-O-C) cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 4.10 (H-2), 3.95 (H-3, $^3J_{H\text{-}2,\ H\text{-}3}$=5.2 Hz), 3.92 (H-5, $^3J_{H\text{-}4,\ H\text{-}5}\cong$6 Hz), 3.89 (H-4), 3.88 (A), 3.83 (B) (H-1,$^3J_{H\text{-}1A,\ H\text{-}2}$=4.7 Hz, $^3J_{H\text{-}1B,\ H\text{-}2}$=3.9 Hz), 3.84 (A), 3.69 (B) (H-6, $^3J_{H\text{-}5,\ H\text{-}6A}$=2.6 Hz, $^3J_{H\text{-}5,\ H\text{-}6B}$=3.9 Hz), 3.68 (A), 3.49 (B) ($^3J_{gem}$=9.0 Hz), 3.60, 3.55 (CH_3CH_2-), 1.215 (CH_3CH_2-, $^3J_{vic}$=6.9 Hz), 1.213 ppm ($\underline{CH_3}CH_2$-, $^3J_{vic}$=6.9 Hz). ^{13}C NMR ($CDCl_3$) δ 84.86 (C-3), 83.67 (C-5), 83.24 (C-4), 80.26 (C-2), 65.64 ($CH_3\underline{CH_2}$-), 62.87 (C-6), 61.81 (C-1), 15.45, 15.31 ppm ($\underline{CH_3}CH_2$-). *Anal.* Calcd for $C_{10}H_{20}O_5$: C, 54.53; H, 9.15. Found: C, 53.93; H, 9.40.

2,5-Anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol (77). The methylation of **66** by use of dimethyl sulfate gave a 81% yield of **77**: ^1H NMR (90 MHz, $CDCl_3$) δ 4.15-3.40 (m, 12H), 3.38 (s, 6H, OCH_3), and 1.19 ppm (dt, 6H, -$CH_2\underline{CH_3}$); IR (film) 2970, 2910, 2875, 2801 (ν, C-H), and 1101 (ν_{as}, C-O-C) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.04 (H-5, $^3J_{H\text{-}6A,H\text{-}5}$=6.0Hz, $^3J_{H\text{-}6B,H\text{-}5}$=4.7Hz, $^3J_{H\text{-}5,H\text{-}4}$=3.9Hz), 3.85 (H-2, $^3J_{H\text{-}2,H\text{-}1A}$=6.0Hz, $^3J_{H\text{-}2,H\text{-}1B}$=6.0Hz, $^3J_{H\text{-}3,H\text{-}2}$=3.4Hz), 3.70 (H-4, $^3J_{H\text{-}5,H\text{-}4}$=3.9Hz, $^3J_{H\text{-}4,H\text{-}3}$<0.5Hz), 3.64 (H-3, $^3J_{H\text{-}3,H\text{-}2}$=3.0Hz, $^3J_{H\text{-}4,H\text{-}3}$<0.5Hz), 3.51 (A) and 3.55 (B) (H-6, $^3J_{H\text{-}6A,H\text{-}5}$=6.9Hz, $^3J_{H\text{-}6B,H\text{-}5}$=4.7Hz, $^3J_{H\text{-}6A,H\text{-}6B}$=9.8Hz), 3.41 (A) and 3.46 (B) (H-1, $^3J_{H\text{-}2,H\text{-}1A}$=5.6Hz, $^3J_{H\text{-}1A,H\text{-}1B}$=9.9Hz), 3.38 (A) and 3.55 (B) (CH_3CH_2-, $^3J_{vic}$ =6.9Hz, $^3J_{gem}$=9.0Hz), 3.45 (A) and 3.50 (B) (CH_3CH_2-), 3.31 (CH_3O-), 1.13 (CH_3CH_2-, $^3J_{vic}$ =6.9Hz), and 1.12 ppm (CH_3CH_2-, $^3J_{vic}$ =6.9Hz); ^{13}C NMR ($CDCl_3$) δ 84.3 (C-3), 83.1 (C-4), 82.2 (C-2), 79.7 (C-5), 73.1 (C-1), 70.7 (C-6), 65.0, 64.9 ($CH_3\underline{CH_2}$-), 59.0 ($\underline{CH_3}O$-), and 15.1 ppm ($\underline{CH_3}CH_2$-); *Anal.* Calcd for $C_{12}H_{24}O_5$: C, 58.04; H, 9.74. Found: C, 58.02; H, 9.76.

Polymerization. A typical polymerization procedure is presented here. Monomer **61** (501.5 mg, 2.48 mmol) was dissolved in dry CH_2Cl_2 (5 mL), and BF_3•OEt_2 (3.1 mL, 0.02 mmol) was added by use of a microsyringe. After 24 h at -30 °C, the solution was poured into a methanol containing a drop of aqueous ammonia, and the resulting solution was replaced by *n*-hexane. The precipitate was isolated and dried under vacuum to yield polymer **79** (190.9 mg, 38%). IR (film) 2960, 2920, 2890, 2860 (ν, C-H), and 1100 (ν_{as}, C-O-C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 4.10, 3.93, 3.80-3.33, and 1.19 ppm. ^{13}C NMR ($CDCl_3$) δ 84.34, 83.15, 82.56, 82.43, 79.84, 72.06, 71.87, 69.40, 65.20, and 15.34 ppm. The specific rotation of polymer **2** in $CHCl_3$ (c 1.14) at 22 °C: $[\alpha]_D$ +32.7°, $[\alpha]_{577}$ +33.3°, $[\alpha]_{546}$ +37.3°, $[\alpha]_{435}$ +60.4°, and $[\alpha]_{405}$ +71.4°.

Cation-binding ability. Metal picrate extractions were carried out using a similar procedure as the one developed by Pedersen[9]. Dye extractions[1] were performed by using equivolumes of the dye (0.1 mg in 10 mL of H_2O) and polymer **78** or polymer **79** (10 mg in 10 mL of CH_2Cl_2) solution.

(*S*,*S*)-1,2:3,4-Butanedioxide (81). The procedure was employed that reported by Seebach et al.[7] To 55 g (0.34 mol) of 2,3-*O*-isopropylidene-L-threitol **85** in 380 mL of dry pyridine was added 140 g (0.73 mol) of *p*-toluenesulfonyl chloride to yield 156.3 g (98%) of 1,4-ditosyl-2,3-*O*-isopropylidene-L-threitol **87**. After recrystallization from ethanol were added 330 mL of 2*N* hydrochloric acid and 670 mL methanol. This solution was refluxed with magnetic stirring for 4 h. The cooled product was neutralized with potassium hydroxide and extracted with chloroform. The solvent was removed under reduced pressure. The product yielded 37 g as liquid. This dihydroxy-ditosylate **87** was treated with potassium hydroxide to close ring. Dioxide **81** yielded 4.8 g (64%), bp 46-49 °C / 17 mmHg. $[\alpha]_D^{20}$=+28.20° (*c*=6.75 in CCl_4). IR (film): 839, 911 cm^{-1} (epoxy). ^1H NMR ($CDCl_3$) δ 2.74-2.91 (m; 6H). *Anal.* Calcd for $C_4H_6O_4$: C, 55.80; H, 7.03. Found: C, 55.65; H, 7.09.

Polymerization of (*S*,*S*)-1,2:3,4-butanedioxide (81). The polymerization was carried out with tin(Ⅳ) chloride or boron trifluoride

etherate as cationic polymerization catalyst and with potassium *tert*-butoxide as anionic catalyst.

Molecular mechanics of force field calculations. Programs MM2 and MM2UEC were used throughout all this work for computation of the geometry and the energy of each conformer for **75** and **77**. The averaged coupling constants was computed by the 3JHH program[25] which is based on Altona's generalized Karplus equation.[26]

Transport experiment. In a "U-tube" with a 14 mm internal diameter was placed 10 mL of chloroform with 2 $g \cdot L^{-1}$ of the host polymer **78**. An aqueous solution (5 mL) containing 0.08 M HCl and 0.02 M guest amine salt, was placed in the α-arm (the source phase). The β-arm (the receiving phase) contained 5.0 mL of 0.10 M HCl solution in water. The chloroform phase was mixed using a small magnetic stirrer at a constant rate. The transported guest salts were followed by measuring the UV absorbance at 272 nm for the solution in the β-arm. The optical purity was determined by HPLC using CROWNPAK CR (+) (Daicel Chemical Industries, Ltd.) as the optical resolution column and aq. $HClO_4$ (pH 2.0) as the eluent.

5.7 References and Notes

(1) For example, *Host Guest Complex Chemistry Macrocycles, -Synthesis, Structures, Applications*-; Vögtle, F.; Weber, E.; Ed.; Springer-Verlag: Berlin, 1985.

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(10) Since a solvent effect was not observed clearly as shown in Table 5.1, it may be pointed out that propagation occurred by S_N2 reaction.

(11) The nucleophilic reaction is an S_N2 reaction for most cyclic ethers. This has been reported by Saegusa and co-worker. Saegusa, T.; Motoi, M.; Suda, H. *Macromolecules*, **1979**, 9, 231.

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6

Conclusion

6.1 Control on Primary Structure of Macromolecular Ionophore via Cyclopolymerizations of Diepoxides and Diepisulfides

Crown ether units have been introduced into the polymer chain by various methods. Since in cyclopolymerization, rings and polymer chain are formed at the same time, polymers with crown units are readily prepared by means of an appropriate molecular design. In chapter 2, the cyclopolymerization of diepoxy compounds namely, 1,2-bis(2,3-epoxypropoxy)benzene, 1,2-bis[2-(2,3-epoxypropoxy)ethoxy]benzene, 5,6:14,15 - dibenzo - 1, 2 : 18, 19- diepoxy - 4,7,10,13,16-pentaoxanonadeca-5,14-diene, and 2,6-bis[3-(4,5-epoxy-2-oxapentyl)-2-methoxy-5-methyl-phenyl]-4-methylanisole gave the polymers, poly([10]crown-3)[1], poly([16]crown-5)[2], poly(dibenzo[19]crown-6)[3], and poly(hemispherand)[4], respectively, which showed the cation-binding properties.

In chapter 3, the cyclopolymerization of diepithio compounds, namely 1,2-bis(2,3-epithiopropoxy)benzene and 1,2-bis[2-(2,3-epithiopropoxy) ethoxy]benzene were carried out to give the polymers with thiacrown ether units containing sulfur atoms. The ring size of the cyclic units in the polymers was fitting to bind metal ions such as Cu^{2+}, Ni^{2+}, Co^{2+}, and Hg^{2+}. This indicated that the characteristics of thiacrown ethers with the sulfide group being a soft base which has a high affinity for soft acids.[5]

These results suggest that the cyclopolymerizations of diepoxides and diepisulfides are a facile method for the syntheses of poly(crown ether)s and poly(thiacrown ether)s with ether and sulfide linkages in the polymer backbone. In addition, it is clear that the method is capable of controlling the primary structure of the polymer with macrocyclic units.

6.2 Control on Secondary Structure of Macromolecular Ionophore via Cyclopolymerization of Chiral Diepoxides

The interest in the chiral compounds which are derived with maintaining chirality from natural products has increased enormously in recent years. In the field of host-guest chemistry, without exception, the synthesis of chiral hosts is a most important concept. In chapter 4, a chiral control was attained in the regio- and stereospecific cyclopolymerization for chiral diepoxy monomers, namely, (*2R,18R*)-(-)- and (*2S,18S*)-(+)-5,6:14,15-dibenzo-1,2:18,19-diepithio-4,7,10,13,16-pentaoxanonadeca-5,14-diene. The polymers, poly[(*R,R*)-dibenzo[19]crown-6] and poly[(*S,S*)-dibenzo[19]crown-6][6], possessed higher stereoregularity, thereby indicating chiral recognition property. The cyclopolymerization of chiral diepoxy monomers is also a facile method for the synthesis of chiral poly(crown ether)s. The method, thus, is capable of controlling the secondary structure of polymers.

6.3 Control on Tertiary Structure of Macromolecular Ionophore via Cyclopolymerization of Diepoxides

Finally, in chapter 5, the polymer with tetrahydrofuranyl repeating units like naturally occurred antibiotic ionophores, such as monensin, nigericin, antibiotic X-206, and alborixin was prepared. The monomer, 1,2;5,6-dianhydro-D-mannitol, derived from natural sugar was cyclopolymerized to give the polymer with 2,5-anhydro-D-glucitol units. The polymer, therefore, is a new family of macromolecular ionophore which belongs to polyether ionophore consisting of a linear array of tetrahydrofuranyl rings.[7] The polymer formed a helical conformer in the complexation with cations, which were able to effectively bind various cations, such as methylene blue and rhodamine 6G, by varying size in the helical cavity. The result indicates a possibility of the control on the tertiary structure of the polymer that is one of the most important aspects in the field of host-guest chemistry.[8]

6.4 Contribution in the Field of Host-Guest Chemistry

As described above, control on primary, secondary, and tertiary structure of polymer was accomplished by the cyclopolymerization of diepoxides and related compounds. In chapter 2, 3, and 4, it was elucidated that the cyclopolymerization is a facile method for syntheses of the host polymers with maclocyclic units.

In chapter 5, a new family of macromolecular ionophore was demonstrated. In general, a linear polymer is able to vary its conformation according to the conditions of polymerization and environment. In many conformations, the unique and interesting form is helical. The helical conformation consists of right- and left-handed turns, each of which is optically active. The biopolymers, such as proteins and nucleic acid have the helical structure with intra and intermolecular hydrogen bonds. The helical structure played an important acts for biological functions.

The macromolecular ionophores described in this thesis possesses a helical structure plays an important act for biological functions. The macromolecular ionophores under consideration possesses a helical structure in complexation with guest. The ionophores presents a new type of hosts in the field of host-guest chemistry.

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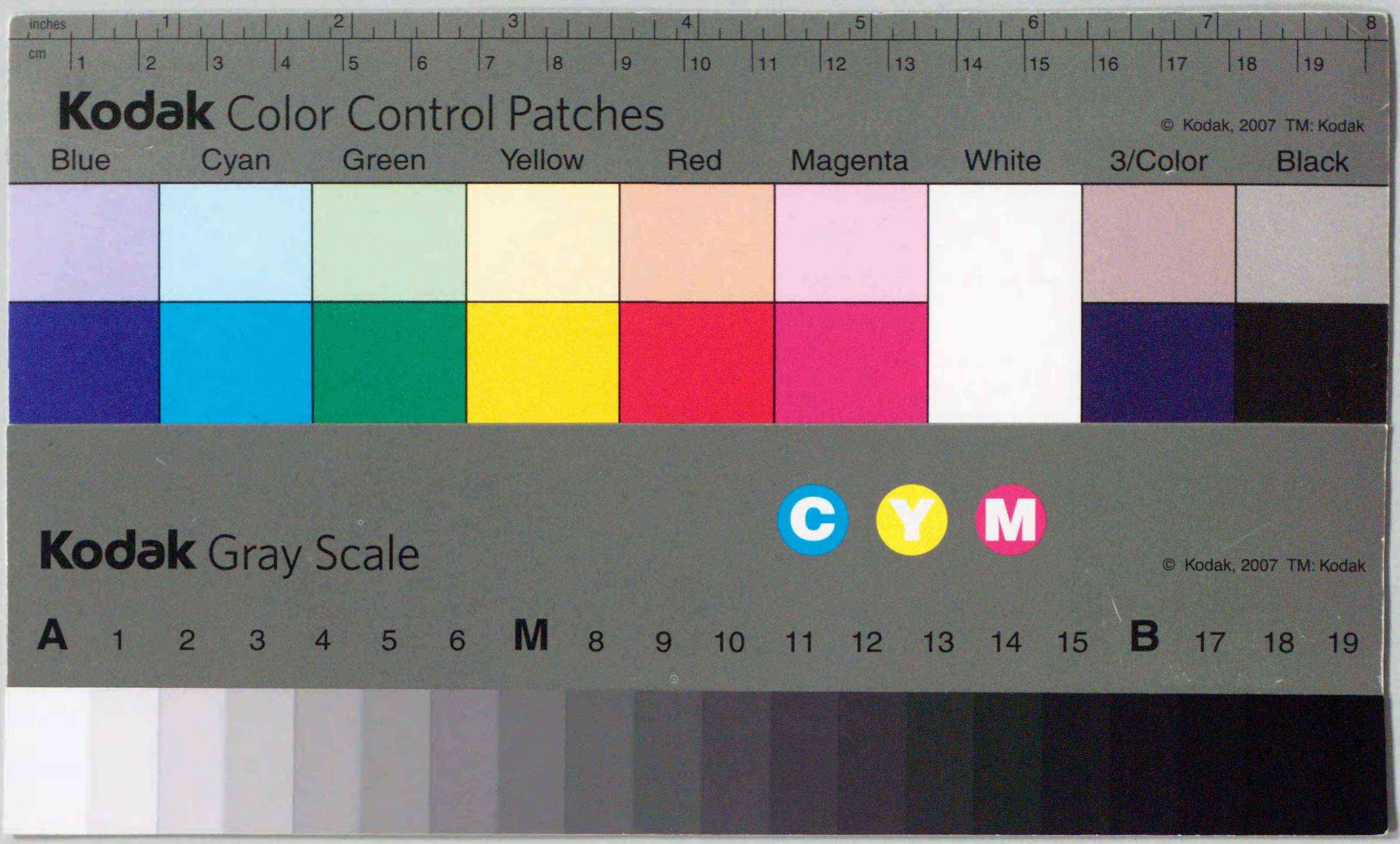
Hisaho Hashimoto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