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

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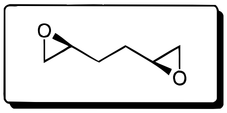
ABSTRACT: The cyclopolymerizations of (2*S*,5*S*)-1,2:5,6-diepoxyhexane using $BF_3{\cdot}OEt_2$ and *tert*-BuOK have been studied. The polymer yield and molecular weight of the polymer using *tert*-BuOK were higher than those using $BF_3{\cdot}OEt_2$. For the polymers using $BF_3{\cdot}OEt_2$, the mole fractions of the cyclized units were 0.76−0.90, and the cyclic constitutional repeating units were five- and six-membered rings. The polymer using *tert*-BuOK essentially consisted of the five-membered cyclic repeating unit.

Introduction

We have studied the regio- and stereoselectivity of the cyclopolymerization of 1,2:5,6-dianhydrohexitol as a new method for producing a carbohydrate polymer.[1−5] The cyclic constitutional units in the resulting polymers depended on the nature of the catalysts used. 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol (**L-1**) and D-mannitol (**D-1**) were cyclopolymerized using $BF_3{\cdot}OEt_2$ and $SnCl_4$ to yield polymers consisting mainly of 2,5-anhydro-D-glucitol recurring units along with the other cyclic ones.[4] In addition, the polymerization using potassium *tert*-butoxide was highly regio- and stereoselective for producing (1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol.[3] However, the polymer yield and molecular weight obtained for **D-1** were higher than those for **L-1**. Therefore, an optically active 1,2:5,6-diepoxyhexane, which corresponds to the dimethoxy group-free **D-1** or **L-1**, is interesting in its cyclopolymerization tendency such as the regio- and stereoselectivity and molecular weight of resulting polymers.

The enantiomeric and diastereomeric mixtures of 1,2:5,6-diepoxyhexane (**(2*SR*,5*RS*)-1**) have been studied with regard to their cyclization and cyclopolymerization. Wiggins et al. reported that **(2*SR*,5*RS*)-1** treated with boiling water formed 2,5-bis(hydroxymethyl)tetrahydrofuran.[6] For the cyclopolymerization of **(2*SR*,5*RS*)-1**, the cyclic repeating units in the resulting polymers were discussed by comparison of the IR and ^{1}H NMR spectra between the polymers and cyclic model compounds. Stille et al. reported that **(2*SR*,5*RS*)-1** was polymerized using cationic and heterogeneous anionic initiators to produce polymers consisting of tetrahydropyran as the cyclic constitutional unit.[7] On the other hand, Bauer reported the polymer consisting of tetrahydrofuran moieties was obtained using a soluble anionic initiator.[8] This ambiguity regarding polymer structure can be clarified using the optically pure isomer of **(2*SR*,5*RS*)-1** and ^{13}C NMR spectral measurements.

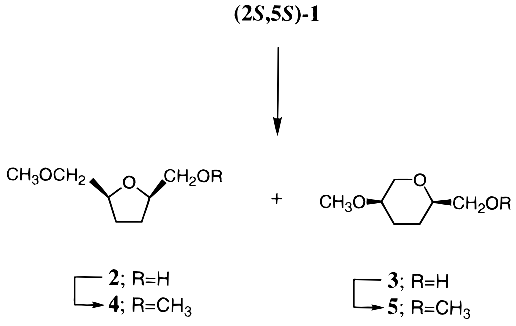
In this paper, we report the cyclopolymerization of (2*S*,5*S*)-1,2:5,6-diepoxyhexane (**(2*S*,5*S*)-1**) using $BF_3{\cdot}OEt_2$ and *tert*-BuOK.



(2*S*,5*S*)-1

For estimating the cyclization tendency, the methanolysis of **(2*S*,5*S*)-1** was carried out using a catalytic amount of hydrochloric acid. After separating the reaction compounds, (2*R*,5*S*)-2-(hydroxymethyl)-5-(methoxymethyl)-tetrahydrofuran (**2**) and (2*R*,5*R*)-2-(hydroxymethyl)-5-methoxytetrahydropyran (**3**) are obtained as the five- and six-membered cyclic unimers, respectively. The structures of the cyclic repeating units in the resulting polymers are confirmed by comparing their ^{13}C NMR spectra with those of (2*R*,5*S*)-2,5-bis(methoxymethyl)-tetrahydrofuran (**4**) and (2*R*,5*R*)-2-(methoxymethyl)-5-methoxytetrahydropyran (**5**) prepared from the methylation of **2** and **3**, respectively.

Scheme 1



Experimental Section

Measurements. ^{1}H and ^{13}C NMR spectra were recorded using a JEOL JNM-EX270 instrument. Optical rotations were determined using a Jasco DIP-140 digital polarimeter. The molecular weight of the resulting polymers was measured by gel permeation chromatography (GPC) in tetrahydrofuran on

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Table 1. Cyclopolymerization of (2*S*,5*S*)-1,2:5,6-Diepoxyhexane ((2*S*,5*S*)-1) using $BF_3{\cdot}OEt_2$ and *tert*-BuOK

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

[a] [**(2*S*,5*S*)-1**]/[$BF_3{\cdot}OEt_2$] = 100; temperature, 0 °C; time, 48 h. [b] [**(2*S*,5*S*)-1**]/[*tert*-BuOK] = 25; temperature, 60 °C; time, 48 h. [c] f_c, the mole fraction of cyclized units in the polymer, determined from the ^1H NMR spectrum. [d] Measured in THF by GPC using polystyrene as standard. [e] Measured in $CHCl_3$ (*c* 1.0). [f] Organic solvent-insoluble polymer was 31.8%. [g] Organic solvent-insoluble polymer was 46.3%.

a Jasco HPLC system equipped with three polystyrene gel columns (Shodex KF-804L). The number-average molecular weight (M_n) was calculated on the basis of a polystyrene calibration.

Materials. (2*S*,5*S*)-1,2:5,6-Diepoxyhexane (**(2*S*,5*S*)-1**) was prepared by the procedure of Machinaga et al.:[9] bp 98−101 °C (25 mmHg) (lit. bp 76 °C (16 mmHg)); $[\alpha]_D$ −23.7° (*c* 1.0, $CHCl_3$) (lit. $[\alpha]_D$ −26.4° (*c* 1.86, $CHCl_3$)); ^1H NMR ($CDCl_3$) δ 2.93−3.02 (m, CH, 2H), 2.78 (dd, J = 4.8 Hz, J = 4.1 Hz, CH_2O, 2H), 2.51 (dd, J = 5.0 Hz, J = 2.6 Hz, CH_2O, 2H), 1.60−1.85 (m, CH_2, 4H); ^{13}C NMR ($CDCl_3$) δ 51.59 (CH), 47.05 (CH_2O), 28.73 (CH_2). Boron trifluoride etherate ($BF_3{\cdot}OEt_2$) was purified by distillation of a commercial product under reduced pressure and used as a solution in dry dichloromethane. Potassium *tert*-butoxide (*tert*-BuOK) was purified by sublimation under vacuum before use. Dichloromethane, 1,4-dioxane, and toluene were purified by the usual methods, and dichloromethane was distilled over calcium hydride and 1,4-dioxane and toluene from sodium−benzophenone ketyl.

Cyclopolymerization. The polymerization using $BF_3{\cdot}OEt_2$ and *tert*-BuOK were carried out following a procedure similar to that reported in previous papers.[3,4]

Model Cyclization. A solution of **(2*S*,5*S*)-1** (1.0 g, 8.76 mmol) in methanol (100 mL) containing a drop of hydrochloric acid was stirred at room temperature for 24 h. The mixture was neutralized by adding methanolic sodium methoxide and then evaporated under reduced pressure. The residue was purified by column chromatography with ethyl acetate/diethyl ether (1/1) to yield (2*R*,5*S*)-2-(hydroxymethyl)-5-(methoxymethyl)tetrahydrofuran (**2**) (0.54 g, 41%) and (2*R*,5*R*)-2-(hydroxymethyl)-5-methoxytetrahydropyran (**3**) (0.45 g, 34%). **2**: $[\alpha]_D$ −11.2° (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.75−2.00 (m, CH_2, 4H), 2.80 (s, OH, 1H), 3.35−3.48 (m, CH_2OCH_3, 2H), 3.40 (s, OCH_3, 3H), 3.53 (dd, J = 9.9 Hz, J = 3.6 Hz, CH_2OH, 1H), 3.76 (d, J = 11.6 Hz, CH_2OH, 1H), 4.05−4.17 (m, CH, 2H); ^{13}C NMR ($CDCl_3$) δ 27.05 (CH_2), 27.94 (CH_2), 59.11 (OCH_3), 65.16 (CH_2OH), 75.11 (CH_2OCH_3), 78.35 (CH), 80.15 (CH). Anal. Calcd for $C_7H_{14}O_3$: C, 57.51; H, 9.65. Found: C, 57.72; H, 9.37. **3**: $[\alpha]_D$ +17.4° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.34−1.39 (m, CH_2, 1H), 1.60−1.69 (m, CH_2, 2H), 2.06−2.13 (m, CH_2, 1H), 2.61 (s, OH, 1H), 3.26 (s, CH, 1H), 3.37 (s, OCH_3, 3H), 3.45−3.56 (m, CH, 1H), 3.51 (dd, J = 12.4 Hz, J = 1.5 Hz, CH_2O, 1H), 3.56−3.59 (m, CH_2OH, 2H), 4.07−4.14 (m, CH_2O, 1H); ^{13}C NMR ($CDCl_3$) δ 22.01 (CH_2), 25.81 (CH_2), 56.07 (OCH_3), 65.88 (CH_2OH), 68.92 (CH_2O), 73.22 (CH), 77.94 (CH). Anal. Calcd for $C_7H_{14}O_3$: C, 57.51; H, 9.65. Found: C, 57.14; H, 9.37.

(2*R*,5*S*)-2,5-Bis(methoxymethyl)tetrahydrofuran (4). To a stirred solution of **2** (0.20 g, 1.8 mmol) in 10 mL of dimethyl sulfoxide were simultaneously added a solution of sodium hydroxide (0.30 g, 7.5 mmol) in 0.3 mL of water and dimethyl sulfate (0.50 g, 4.0 mmol) at such a rate that the temperature of the reaction mixture did not exceed 60 °C. Stirring was continued at this temperature for 30 min. After standing overnight at room temperature, the mixture was poured into water and extracted with chloroform. The extract was dried, and the residue was purified by column chromatography with *n*-hexane/diethyl ether (1/3) to give **4** (77 mg, 35%): ^1H NMR ($CDCl_3$) δ 1.58−1.74 (m, CH_2, 2H), 1.88−2.03 (m, CH_2, 2H), 3.32−3.45 (m, CH_2O, 4H), 3.38 (s, OCH_3, 6H), 4.08 (ddd, J = 7.1 Hz, J = 5.1 Hz, J = 2.1 Hz, CH, 2H); ^{13}C NMR ($CDCl_3$) δ 27.77 (CH_2), 59.23 (OCH_3), 75.43 (CH_2O), 78.37 (CH). Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 59.81; H, 10.01.

(2*R*,5*R*)-2-(Methoxymethyl)-5-methoxytetrahydropyran (5). The synthetic procedure is the same as that for **4**: Yield: 57 mg (26%); $[\alpha]_D$ +40.6° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.37−1.45 (m, CH_2, 1H), 1.56−1.72 (m, CH_2, 2H), 2.00−2.14 (m, CH_2, 1H), 3.24−3.64 (m, CH_2OCH_3, CH, 4H), 3.37 (s, OCH_3, 3H), 3.38 (s, OCH_3, 3H), 3.50 (dd, J = 12.5 and 1.3 Hz, CH_2O, 1H), 4.25 (ddd, J = 12.4 Hz, J = 4.3 Hz, J = 2.1 Hz, CH_2O, 1H); ^{13}C NMR ($CDCl_3$) δ 22.84 (CH_2), 26.35 (CH_2), 56.09 (OCH_3), 59.18 (OCH_3), 68.74 (OCH_2), 73.20 (CH), 76.08 (CH_2OCH_3), 76.50 (CH). Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 59.72; H, 9.33.

Results and Discussion

Table 1 lists the results of the polymerization of (2*S*,5*S*)-1,2:5,6-diepoxyhexane (**(2*S*,5*S*)-1**) using $BF_3{\cdot}OEt_2$ and *tert*-BuOK. After $BF_3{\cdot}OEt_2$ was added to the monomer solution with the monomer concentration ([M]) of 0.5 mol·L^{-1}, the polymerization system became immediately heterogeneous. Approximately half of the resulting polymer was soluble in chloroform and THF, but the rest was insoluble. On the other hand, the polymerization at the [M] of 0.2 mol·L^{-1} proceeded homogeneously to give the organic solvent-soluble polymer. Number-average molecular weights (M_n) were 1300−3600, corresponding to number-average degrees of polymerization (DP_n) of 11.4−31.6. Specific rotations ($[\alpha]^{22}_D$) ranged from +3.0 to +7.2° (*c* 1.0 in $CHCl_3$ at 22 °C).

For the polymerization using *tert*-BuOK, the catalyst gradually dissolved into the polymerization system after several hours and the system turned brown. Although the [M] was higher than that using $BF_3{\cdot}OEt_2$, the polymerization proceeded homogeneously to give the organic solvent-soluble polymers in high yields. The M_n's of 6300 and 6500, which corresponded to DP_n's of 55.2 and 56.9, respectively, were higher than those using $BF_3{\cdot}OEt_2$. The specific rotation ($[\alpha]^{22}_D$) was −1.6° (*c* 1.0 in $CHCl_3$ at 22 °C) and its sign was opposite of that for the polymer using $BF_3{\cdot}OEt_2$.

Figure 1 shows the ^1H NMR spectra of the polymers obtained using $BF_3{\cdot}OEt_2$ and *tert*-BuOK. The characteristic absorptions at 2.51 and 2.78 ppm due to the epoxy groups were observed, so the polymer using $BF_3{\cdot}OEt_2$ contained unreacted epoxy groups. The mole fractions of cyclized units in the polymer (f_c), which was determined from the relative peak areas of the protons in the ^1H NMR spectra, were 0.76−0.90. On the contrary, since the ^1H NMR spectra of the polymers using *tert*-BuOK indicated the absence of the epoxy groups, the polymerization proceeded according to a cyclopolymerization mechanism leading to the polymers consisting of cyclic constitutional repeating units, i.e., an f_c of >0.99.

The ^{13}C NMR spectrum of the polymer obtained using *tert*-BuOK showed clearly three signals at 78.40, 74.23, and 27.92 ppm, which were assigned to the CH, OCH_2, and CH_2 carbons, respectively, as shown in Figure 2. For the polymer with $BF_3{\cdot}OEt_2$, similar signals marked

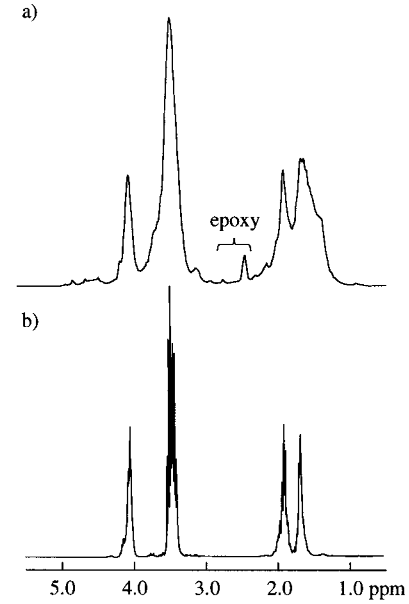


Figure 1. ^{1}H NMR spectra of the polymers prepared from (2*S*,5*S*)-1,2:5,6-diepoxyhexane (**(2*S*,5*S*)-1**) using $BF_3{\cdot}OEt_2$ in CH_2Cl_2 (a) and *tert*-BuOK in toluene (b).

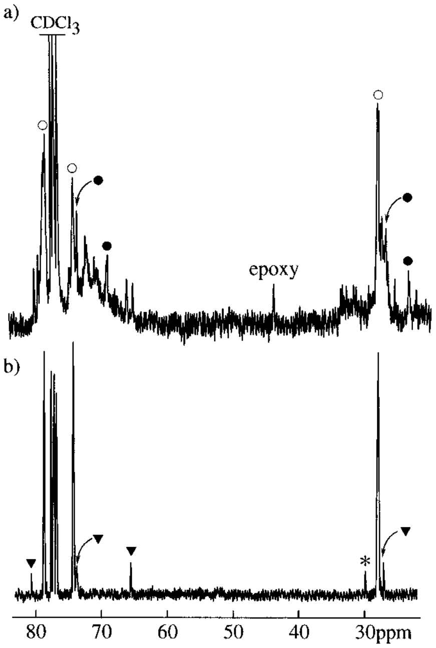


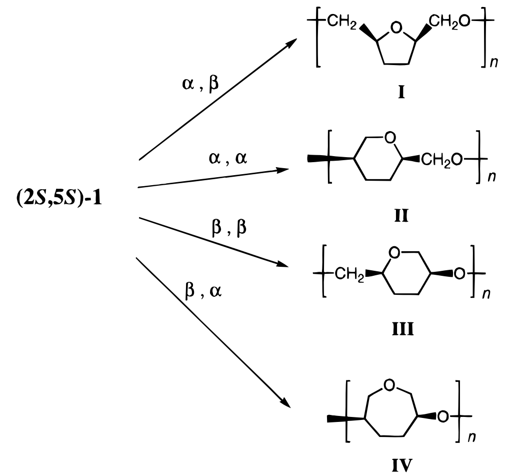
Figure 2. ^{13}C NMR spectra of the polymers prepared from (2*S*,5*S*)-1,2:5,6-diepoxyhexane (**(2*S*,5*S*)-1**) using $BF_3{\cdot}OEt_2$ in CH_2Cl_2 (a) and *tert*-BuOK in toluene (b).

with the open circles were also observed at 78.37, 74.14, and 27.86 ppm. In addition, there are multiple small absorptions along with the signal at 43.83 ppm due to the residual epoxy carbon.

These NMR spectral measurement results indicate that the polymer structure obtained using *tert*-BuOK was highly regio- and stereoselective, while that using $BF_3{\cdot}OEt_2$ was irregular. This was very similar to the cyclopolymerization tendency of **L-1** and **D-1** using $BF_3{\cdot}OEt_2$ and *tert*-BuOK.[3,4]

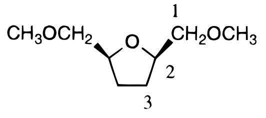
For the cationic polymerization of monosubstituted epoxides through an S_N2-type mechanism, the configuration of the asymmetric carbon atom is inverted due to the ring-opening at the CH−O bond (α-scission) and retention by the CH_2−O bond (*β*-scission). On the other hand, the anionic polymerization exclusively proceeds through *β*-scission. For the polymerization of **(2*S*,5*S*)-1**, Scheme 2 represents the possible cyclic units. The intramolecular cyclization and the intermolecular reaction through α,α- and *β*,*β*-scissions of the two epoxides in a monomer molecule form the six-membered rings **II** and **III**, respectively, whereas α,*β*- and *β*,α-scissions lead to the formation of the five- and seven-membered rings **I** and **IV**, respectively.

Scheme 2[a]



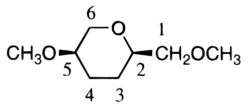
[a] The former and latter symbols correspond to the intramolecular and intermolecular scissions, respectively.

Chart 1



4

C	δ/ppm
1	75.43
2	78.37
3	27.77
CH$_3$O	59.23



5

C	δ/ppm
1	76.08
2	76.50
3	22.84
4	26.35
5	73.20
6	68.74
CH$_3$O	56.09
CH$_3$O	59.18

In order to estimate the cyclization tendency using a cationic catalyst, **(2*S*,5*S*)-1** was reacted in MeOH using a catalytic amount of hydrochloric acid. (2*R*,5*S*)-2-(Hydroxymethyl)-5-(methoxymethyl)tetrahydrofuran (**2**) and (2*R*,5*R*)-2-(hydroxymethyl)-5-methoxytetrahydropyran (**3**) were obtained as the cyclic unimers in the ratio of 8/7. In addition, they were methylated to (2*R*,5*S*)-2,5-bis(methoxymethyl)tetrahydrofuran (**4**) and (2*R*,5*R*)-2-(methoxymethyl)-5-methoxytetrahydropyran (**5**) for confirming the cyclic structures in the polymers. The chemical shifts of the ^{13}C NMR signals for **4** and **5** are summarized in Chart 1.

The signals at 78.37, 74.14, and 27.86 ppm for the polymer obtained using $BF_3{\cdot}OEt_2$ were very close to the chemical shift values of 78.37 (CH), 75.43 (CH_2O), and 27.77 ppm (CH_2) for **4**; therefore, the main cyclic structure was the five-membered ring **I**. In addition, because the absorptions marked with the solid circles were similar to the chemical shifts for **5**, the six-membered ring **II** should be contained in the polymer. However, many other smaller signals were observed and their assignments were not clear. The polymer using $BF_3 \cdot OEt_2$ consisted of the five- and six-membered rings as cyclic units along with a pendant epoxy group unit. This structural characteristic is consistent with the cationic cyclization tendency of **(2*S*,5*S*)-1** in which the five- and six-membered cyclic unimers, **2** and **3**, are simultaneously formed.

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

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

We have recently proposed that the regio- and stereoselective cyclopolymerization of 1,2:5,6-dianhydrohexitol using an anionic catalyst is a new synthetic strategy for artificial polycarbohydrates, which is exactly opposite from the ring-opening polymerization of the anhydro sugar.[3] This method is found to be applicable to 1,2:5,6-dianhydro-3,4-dideoxy-D-mannitol, i.e., (2*S*,5*S*)-1,2:5,6-diepoxyhexane (**(2*S*,5*S*)-1**).

Conclusion

The cyclopolymerizations of **(2*S*,5*S*)-1** using $BF_3 \cdot OEt_2$ and *tert*-BuOK were carried out. For the polymer obtained using $BF_3 \cdot OEt_2$, the cyclic constitutional repeating units were the five- and six-membered rings together with a pendant epoxy group unit. The polymer using *tert*-BuOK essentially consisted of the five-membered cyclic repeating unit. These results clarified the ambiguity on the polymer structures for the cationic and anionic cyclopolymerizations of **(2*SR*,5*RS*)-1**.

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