

## NOTE

# Synthesis of Optically Active Polyamines Based on Chiral 1-Cyclohexylethylamine Derivatives

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Recently, the precise control of macromolecular architectures has attracted considerable attention. Optically active polymers<sup>1</sup> often play important roles as key building blocks for well-defined polymers having specific higher-ordered structures. These polymers, therefore, have considerable potential for applications in the development of novel materials. In particular, chiral chromatography columns<sup>2</sup> and gas permselective membranes<sup>3</sup> based on these polymers are of considerable industrial importance. A variety of artificial optically active polymers, excluding bio-related polymers, such as polymethacrylate,<sup>4</sup> polyacrylamide,<sup>5</sup> polyisocyanate,<sup>6</sup> polyacetylene,<sup>7</sup> polysilane,<sup>8</sup> etc., have attracted considerable attention in this regard. It is very important to extend the scope of synthetic approaches to optically active polymers for the development of novel materials in the future. From a synthetic viewpoint, chiral monomer polymerization is a useful process because of the wide applicability of monomer, apart from both asymmetric polymerization of achiral or prochiral monomers and enantioselective polymerization of a racemic monomer.<sup>9</sup> In this paper, we report on new optically active polymers having chiral auxiliary in the side chain prepared by the polycondensation of chiral 1-cyclohexylamine or 1-phenylethylamine with *p*-xylylene dibromide. The nitrogen atoms in the polymer backbone are expected to initiate the formation of a higher-ordered structure *via* inter- or intramolecular interaction and a ligand for molecular recognition.<sup>10</sup>

## EXPERIMENTAL

### General

Unless otherwise noted, all reagents and chemicals were used without further purification. *p*-Xylylene dibromide, benzylbromide, 1-cyclohexylethylamines, and 1-phenylethylamines were obtained from TCI. 2,6-Dimethylnaphthalene and 2-bromomethylnaphthalene were obtained from Wako Pure Chem and Aldrich, respectively. All the <sup>1</sup>H NMR spectra (in CDCl<sub>3</sub>-*d*) and the <sup>13</sup>C NMR spectra (in CDCl<sub>3</sub>-*d*) were recorded by a 400 MHz JEOL LNM-EX400 instrument with

tetramethylsilane (TMS) as the internal standard. The FT-IR spectra were recorded using a JASCO FT-IR 460 plus spectrometer. Gel permeation chromatography (GPC) was carried out by a JASCO UV-2070 detector and a JASCO RI-2031 detector (TOSOH TSKgel G3000H<sub>XL</sub> or G4000H<sub>XL</sub> column) using tetrahydrofuran (THF) as the eluent after calibration with polystyrene standards. The solution property of the polymer in a diluted THF solution was examined by a SEC-VISC-RALLS system (Viscotek). Thermogravimetric analysis (TGA) was performed using a SII TG/DTA 6200 machine (SEIKO Instrument Inc.) with a heating rate of 10 °C/min under a nitrogen atmosphere. Differential scanning calorimetry (DSC) was carried out on a SII DSC 6220 at a heating rate of 5 °C/min under a nitrogen atmosphere. CD spectra were taken on a JASCO J-820 spectropolarimeter. Specific optical rotations were measured on a JASCO DIP-1000 digital polarimeter in a 10 cm cuvette.

### General Procedure of Optically Active Polymer (1)

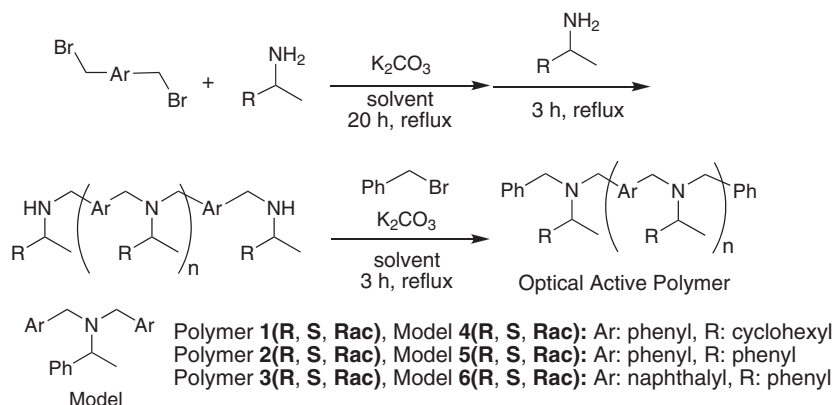
Potassium carbonate (10 mmol) was added to a solution of *p*-xylylene dibromide (2 mmol), (R)-(-)-1-cyclohexylethylamine (2 mmol), and acetonitrile/*o*-dichlorobenzene (2/2 mL) at room temperature. After stirring for 20 h at 90 °C, (R)-(-)-1-cyclohexylethylamine (2 mmol) was added to the resulting solution and stirred for 3 h at 90 °C. After filtration and removal of solvent, the obtained residue was dissolved into minimum volume chloroform, and reprecipitated in methanol. The THF solution of the obtained product and benzyl bromide (2 mmol) in the presence of potassium carbonate (10 mmol) was refluxed for 3 h. The resulting solution was filtered off to remove salt and then concentrated under reduced pressure. The obtained residue was dissolved into minimum volume chloroform, and reprecipitated in methanol. The obtained precipitate was dried *in vacuo* to give the optically active polymer **1**.

**Polymer 1(R).** From (R)-(-)-1-cyclohexylethylamine (0.254 g, 2 mmol), *p*-xylylene dibromide (0.527 g, 2 mmol), Yield 51%;  $M_n = 7600$ ,  $M_w = 17000$ ,  $M_w/M_n = 2.2$ ; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ppm)  $\delta$  7.54–7.27 (4H, Ph-H), 3.85–3.02

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**Scheme 1.** Synthesis of optically active polyamines and model compounds.

(4H, Ph-CH<sub>2</sub>-N) 2.42–2.12, 1.92–0.50 (15H, C<sub>6</sub>H<sub>11</sub>-CH(CH<sub>3</sub>)-N); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz, ppm) δ 139.0, 128.5, 57.1, 53.4, 41.2, 30.8, 30.7, 26.6, 26.5, 26.4; IR (NaCl, cm<sup>-1</sup>): ν = 2920, 2850, 2810, 1510, 1450, 1370, 1140.

**Polymer 1(S).** From (S)-(+)-1-cyclohexylethylamine (0.257 g, 2 mmol), *p*-xylylene dibromide (0.534 g, 2 mmol), Yield 59%; *M<sub>n</sub>* = 6800, *M<sub>w</sub>* = 13000, *M<sub>w</sub>*/*M<sub>n</sub>* = 2.0; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ppm) δ 7.43–7.10 (4H, Ph-H), 3.83–3.08 (4H, Ph-CH<sub>2</sub>-N) 2.40–2.19, 1.81–0.52 (15H, C<sub>6</sub>H<sub>11</sub>-CH(CH<sub>3</sub>)-N); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz, ppm) δ 139.0, 128.5, 57.1, 53.3, 41.1, 30.8, 30.7, 26.6, 26.5, 26.3, 9.20; IR (NaCl, cm<sup>-1</sup>): ν = 2920, 2850, 2810, 1510, 1450, 1370, 1140.

**Polymer 1(Rac).** From (DL)-1-cyclohexylethylamine (0.255 g, 2 mmol), *p*-xylylene dibromide (0.530 g, 2 mmol), Yield 58%; *M<sub>n</sub>* = 9400, *M<sub>w</sub>* = 18000, *M<sub>w</sub>*/*M<sub>n</sub>* = 1.9; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ppm) δ 7.39–7.20 (4H, Ph-H), 3.79–3.17 (4H, Ph-CH<sub>2</sub>-N) 2.40–2.20, 1.76–0.58 (15H, C<sub>6</sub>H<sub>11</sub>-CH(CH<sub>3</sub>)-N); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz, ppm) δ 139.0, 128.5, 57.1, 53.3, 41.1, 30.9, 30.7, 26.6, 26.5, 26.4, 9.10; IR (NaCl, cm<sup>-1</sup>): ν = 2920, 2850, 2810, 1510, 1450, 1370, 1140.

#### General Procedure of Model Compound (4)

Potassium carbonate (50 mmol) was added to a solution of benzyl bromide (4 mmol), (R)-(-)-1-cyclohexylethylamine (2 mmol) and acetonitrile (12 mL) at room temperature. After refluxing for several hours, the mixture was filtered off to remove salt and then the resulting solution was concentrated under reduced pressure. The obtained residue was dissolved into chloroform (10 mL) and washed with water (50 mL × 3) to afford the model compound **4**.

**Model Compound 4(Rac).** From (R)-(-)-1-cyclohexylethylamine (0.24 g, 1.8 mmol), benzylbromide (0.67 g, 3.9 mmol), Yield 80%; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ppm) δ 7.39–7.19 (m, 10H), 3.77, 3.31 (dd, *J* = 13.9, 13.9 Hz, 4H), 2.39–2.28 (m, 2H), 1.67–1.54 (m, 4H), 1.23–1.02 (m, 3H), 0.972 (d, *J* = 6.6 Hz, 3H), 0.78–0.66 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz, ppm) δ 140.7, 128.7, 128.0, 126.5, 57.4, 53.6, 41.2, 30.9, 30.7, 26.6, 26.5, 26.4, 9.20; IR (NaCl, cm<sup>-1</sup>) ν = 3030, 2920, 2850, 1490, 1450, 1380, 1140.

**Model Compound 4(S).** From (S)-(+)-1-cyclohexylethyl-

amine (0.26 g, 2 mmol), benzylbromide (0.69 g, 4.1 mmol), Yield 87%; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ppm) δ 7.39–7.19 (m, 10H), 3.77, 3.31 (dd, *J* = 13.9, 13.9 Hz, 4H), 2.38–2.27 (m, 2H), 1.67–1.55 (m, 4H), 1.23–1.02 (m, 3H), 0.972 (d, *J* = 6.6 Hz, 3H), 0.78–0.66 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz, ppm) δ 140.7, 128.7, 128.0, 126.5, 57.4, 53.6, 41.2, 30.9, 30.7, 26.6, 26.5, 26.4, 9.20; IR (NaCl, cm<sup>-1</sup>) ν = 3030, 2920, 2850, 1490, 1450, 1380, 1140.

**Model Compound 4(Rac).** From (DL)-1-cyclohexylethylamine (0.26 g, 2 mmol), benzylbromide (0.69 g, 4.1 mmol), Yield 92%; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ppm) δ 7.39–7.19 (m, 10H), 3.77, 3.31 (dd, *J* = 13.9, 13.9 Hz, 4H), 2.39–2.28 (m, 2H), 1.67–1.57 (m, 4H), 1.22–1.02 (m, 3H), 0.972 (d, *J* = 6.6 Hz, 3H), 0.78–0.66 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz, ppm) δ 140.7, 128.7, 128.0, 126.5, 57.4, 53.6, 41.2, 30.9, 30.7, 26.6, 26.5, 26.4, 9.20; IR (NaCl, cm<sup>-1</sup>) ν = 3030, 2920, 2850, 1490, 1450, 1380, 1140.

## RESULTS AND DISCUSSION

The typical procedure for the polymerization of chiral amines and dibromides is as follows (Scheme 1): An acetonitrile/*o*-dichlorobenzene (1/1) mixed solution containing an equimolar amount of *p*-xylylene dibromide and (R)-(-)-1-cyclohexylethylamine was vigorously stirred and heated in the presence of K<sub>2</sub>CO<sub>3</sub>, and then, an excess amount of chiral amine was added to the solution. The terminal amine group was end-capped using an excess amount of benzyl bromide to yield a crude material. Further purification was carried out by reprecipitation in a methanol/acetone mixture. The optically active polymer **1R** was obtained as a colorless precipitate. A similar polymerization procedure using other chiral and racemic amines afforded the corresponding polymers **1(S and Rac)**, **2(R, S, and Rac)**, and **3(R, S, and Rac)**. The obtained polymers had low solubility in acetone and acetonitrile, while they had good solubility in tetrahydrofuran (THF) and chloroform. Model compounds of each polymer were also prepared (Scheme 1).

The polymerization results are summarized in Table I. The yields of the polymers were 46%–79%, while their molecular weights *M<sub>n</sub>* found to be 5200–20000 by GPC (eluent: THF;

**Table I.** Properties of optically active polymers

Entry	Product	Yield/%	Molecular Weight					$T_g/^\circ\text{C}$	$T_{d10}/^\circ\text{C}$	$[\alpha]_D^{20c}$	
			GPC <sup>a)</sup>		LS <sup>b)</sup>					Model	Polymer
			$M_n$	PDI	$M_w$	PDI	a				
1	<b>1(R)</b>	51	7600	2.2	17000	1.6	0.68	82	296	-21.8	7.08
2	<b>1(S)</b>	59	6800	2.0	14000	1.3	0.66	90	306	21.6	-6.44
3	<b>1(Rac)</b>	58	9400	1.9	18000	1.3	0.68	93	301	-0.06	-0.07
4	<b>2(R)</b>	46	8600	2.1	21000	1.6	0.64	80	338	98.9	199
5	<b>2(S)</b>	68	18000	1.6	27000	1.2	0.72	81	309	-98.0	-207
6	<b>2(Rac)</b>	79	20000	1.5	34000	1.2	0.73	78	312	-0.442	-3.55
7	<b>3(R)</b>	54	6000	2.1	16000	1.1	0.63	108	339	150	303
8	<b>3(S)</b>	52	5800	2.2	16000	1.2	0.65	109	335	-208	-293
9	<b>3(Rac)</b>	62	5200	2.2	13000	1.1	0.64	106	312	-3.46	-3.41

a) eluent: THF; polystyrene standards. b) Light Scattering (THF). c) Specific Rotation (THF, 20°C, c 0.010 for **6(R)**, **6(S)**, **6(Rac)** and c 0.10 for the others).

polystyrene standards) in each case. The absolute molecular weight ( $M_w$ ) and solution properties were estimated using a SEC-VISC-RALLS system (Viscotek) with an online viscometer (VISC) and a right-angle laser light scattering (RALLS) detector in a diluted THF solution. The polymers were estimated to have  $M_w$  values of 13000–34000, and they exhibited a moderate Mark-Houwink-Sakurada  $a$ -value of *ca.* 0.63–0.73, suggesting that they have a random coil in a solution state, as expected. The thermal properties of the polymers were evaluated by DSC and TGA. The polymers were observed to have a glass transition temperature ( $T_g$ ) ranging between 78–109°C, and they were confirmed to have moderate thermal stability ( $T_{d10}$  = 296–339°C). In each case, no well-defined difference was observed among the **R**, **S**, and **Rac** polymers. The structures of the polymers were determined from their <sup>1</sup>H NMR, <sup>13</sup>C NMR, and FT-IR spectra; the FT-IR spectra indicated that none of the quaternary amines were contaminated. Therefore, the obtained polymers had a linear structure (supporting information Figure S1).

An inspection of the specific rotation data of the optically active polymers (Table I), particularly the rotation values, indicated that in a solution, the polymers take on some higher-order or regular structures that differ from those of the corresponding model compounds. In other words, a comparison of the polymers and model compounds revealed that the specific rotation was inverted from a negative value to a positive value in **1(R)**, **1(S)**, and the specific rotation was approximately twice as high in **2(R)**, **2(S)** and **3(R)**, **3(S)**.<sup>11</sup>

Meanwhile, the Cotton effect was observed in the CD spectra of the **R** and **S** optically active polymers. The **R** and **S** polymers were clearly observed to exhibit opposite Cotton effects; however, a clear Cotton effect was not confirmed in the **Rac** polymers. In particular, although the UV-vis and CD spectra of **1(R)** and **1(S)** were observed to be red-shifted as compared to those of the model compounds **4(R)** and **4(S)**, the Cotton effects of the two model compounds at around 220 nm were weak in both cases, while those for the polymers at around 230 nm were sufficiently larger. This result suggested the generation of some secondary structures in a polymer state (Figure 1).

On the other hand, although the UV-vis and CD spectra were observed to be red-shifted, the Cotton effects of the model compounds were very similar to those of polymers **2(R)**, **2(S)** and **3(R)**, **3(S)**. In these cases, it was not clear whether the main-chain chirality was induced by the polymerization (Figure 2).

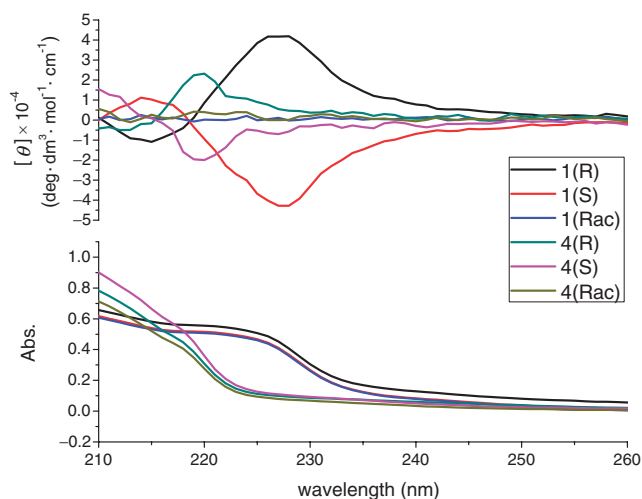
The CD intensity of **1(R)** was observed to have slight temperature dependence (Figure 3). For example, the CD intensity in **1(R)** gradually decreased with increasing temperature; therefore, some secondary structures were disordered at high temperature.<sup>12</sup>

Polyamines can be converted to water-soluble polymers with ammonium salts in the main chain by adding them to the appropriate acid. Polyamine **1(R)** was dissolved in an acidic water solution (3:7 mixed solvent of 0.17 N hydrochloric acid and THF) at a concentration of  $5 \times 10^{-4}$  M. From the CD spectrum, similar CD intensities and Cotton effects were observed in both the THF and acidic water solutions (Figure 3). Therefore, the optically active polyamine also might have some stable secondary structures in the acidic water solution.

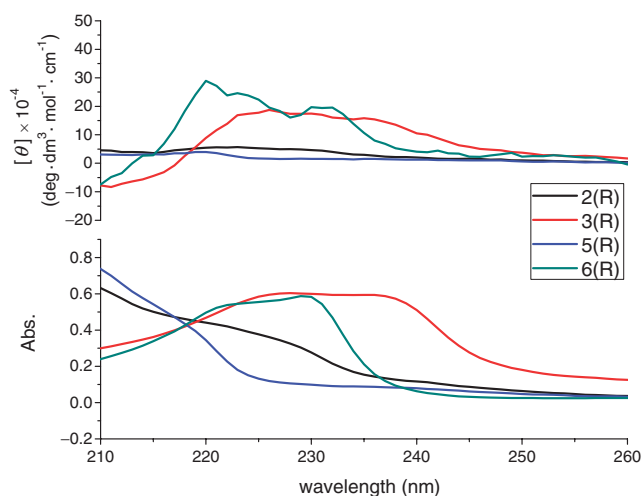
## CONCLUSION

In conclusion, a new optically active polyamine was easily prepared by the polycondensation of chiral 1-cyclohexylethylamine derivatives with *p*-xylylene dibromide in the presence of K<sub>2</sub>CO<sub>3</sub>. Although the detailed structures of the polymers have not yet been clarified, it is possible that they take on some helical structures induced by the introduction of a bulky chiral amine. In addition, the obtained polyamines have considerable potential for applications in the development of novel materials. Future works include the evaluation of the bulk properties of polymers, molecular recognition of chiral compounds, and the investigation of the ability of an additive to fold or unfold some proteins.<sup>13</sup>

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**Figure 1.** CD and UV-vis spectra of polymer **1** and model compound **4** (THF, 20°C, 210–260 nm,  $c$   $5 \times 10^{-4}$  M for **1**,  $c$   $4 \times 10^{-4}$  M for **4**).



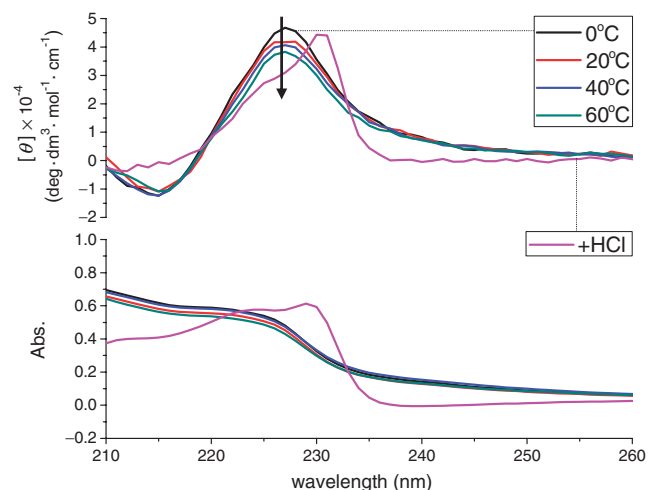
**Figure 2.** CD and UV-vis spectra of polymer **2**, **3** and model compound **5**, **6** (THF, 20°C, 210–260 nm,  $c$   $2.5 \times 10^{-4}$  M for **2** and **5**,  $c$   $1 \times 10^{-4}$  M for **3**,  $c$   $3 \times 10^{-5}$  M for **6**).

*Electronic Supporting Information Available:* Spectral data of polymers and model compounds, Figures S1, S2, S3, S4, and S5. These materials are available via the Internet at <http://www.spsj.or.jp/c5/pj/pj.htm>

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**Figure 3.** Temperature dependency (THF, 20°C, 210–260 nm,  $5 \times 10^{-4}$  M) and additive effect of HCl (THF/0.17 N HCl<sub>aq</sub> = 3/7, 20°C, 210–260 nm,  $5 \times 10^{-4}$  M) on CD spectra of polymer **1(R)**.

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