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Enantiomer-Selective Radical Cyclopolymerization of *rac*-2,4-Pentanediyl Dimethacrylate Using ATRP Initiating System with Chiral Amine Ligand

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For the enantiomer-selective polymerization of a racemic monomer, various examples have been reported based on the ionic and coordination polymerizations; e.g., high enantiomer selectivity was achieved in the anionic polymerization of racemic α-monosubstitued benzyl methacrylates using a (−)-sparteine/Grignard reagent[1−3] and in the ring-opening polymerization of propylene sulfide with (−)-binaphthol/$ZnEt_2$.[4,5] However, there are few studies on enantiomer-selective radical polymerization. Okamoto et al. reported that the radical polymerization of methacrylate with a bulky side group is enantiomer-selective when a very slight excess of one enantiomer is used.[6,7]

Cyclopolymerization is a promising method for synthesizing optically active polymers. The cyclocopolymerization of a divinyl monomer having a chiral template with an achiral vinyl monomer is the most established method.[8,9] In addition, the enantioselective cyclopolymerization of an achiral bifunctional monomer was realized by using a chiral initiating system, such as in the cyclopolymerization of 1,5-hexadiene with a chiral metallocene metal source[10] and the cyclopolymerization of benzaldehyde divinyl acetal with a chiral 10-camphorsulfonic acid/$ZnCl_2$ initiating system.[11] However, the enantiomer-selective cyclopolymerization of a racemic monomer has never been reported. We now report the enantiomer-selective radical cyclopolymerization of a racemic monomer by atom transfer radical polymerization[12] modified with the asymmetric Kharasch−Sosnovsky reaction;[13−16] i.e., we polymerized *rac*-2,4-pentanediyl dimethacrylate (*rac*-**1**) using initiating systems consisting of methyl 2-bromoisobutyrate (**3**), CuBr as the metal source, and hydroxy-1,7,7-trimethylbicyclo[2.2.1]heptan-2-*endo*-yl}-2,2′-bipyridine (**4**),[17] (−)-sparteine (**5**), (*S*,*S*)-2,6-bis(4-isopropyl-2-oxazolin-2-yl)pyridine (*S*-**6**), and (*R*,*R*)-2,6-bis(4-isopropyl-2-oxazolin-2-yl)pyridine (*R*-**6**) as chiral amine ligands, as shown in Scheme 1.

After *rac*-2,4-pentanediol was separated from a mixture of *meso*- and *rac*-2,4-pentanediol by column chromatography on silica gel using diethyl ether as the eluent, *rac*-**1** was synthesized from the reaction of *rac*-2,4-pentanediol and methacryloyl chloride.[18] The atom transfer radical polymerization of *rac*-**1** was carried out using the initiating systems consisting of **3**/CuBr/chiral amine ligands (Table 1).[19] All of the polymerizations were homogeneous, and the resulting polymers were soluble in chloroform and tetrahydrofuran. Because the characteristic methacrylate resonance was not observed in the ^{13}C NMR spectrum of the polymer, the polymerization of *rac*-**1** evidently proceeded through a cyclopolymerization mechanism to afford the polymer essentially consisting of cyclic constitutional repeating units; i.e., the extent of the cyclization was ca. 100%.

Table 1. Polymerization of *rac*-1 Using 3/CuBr/Ligand as an Initiation System[a]

			recovered monomer		polymer **2**	
ligand	time (h)	conv[b] (%)	selected monomer	*e.e.*[b,c] (%)	M_n (M_w/M_n)[d]	$[\alpha]_{435}$[e] (deg)
4	4	26.9	*RR*-**1**	6.8	13 500 (1.23)	−18.9
5	12	18.5	*RR*-**1**	9.4	11 000 (1.30)	−35.5
S-**6**	6	24.6	*RR*-**1**	15.3	12 300 (1.25)	−36.5
R-**6**	6	22.8	*SS*-**1**	13.4	11 200 (1.23)	+38.6

[a] Conditions: $[rac\text{-}\mathbf{1}]_0 = 0.1$ mol L^{-1}; $[rac\text{-}\mathbf{1}]_0/[\mathbf{3}]_0/[\text{CuBr}]_0/[\text{ligand}]_0 = 200/1/2/4$; solvent, anisole; temperature, 90 °C. [b] Determined by HPLC equipped with CHIRALCEL OB-H column. [c] Enantiomeric excess. [d] Determined by GPC in THF using polystyrene standards. [e] Measured in $CHCl_3$ (*c* 0.3, 28 °C).

The number-average molecular weights (M_n) of the resulting polymers ranged from 11 000 to 13 500, and the molecular weight distributions (M_w/M_n) were relatively narrow. The chiral amine ligand affected the enantiomer selectivity; i.e., the enantiomeric excess of the recovered monomer (*e.e.*) was 6.8%−15.3%. In addition, enantiomer selectivity changed with the chirality of the amine ligands used; i.e., (2*S*,4*S*)-2,4-pentanediyl dimethacrylate (*SS*-**1**) enantiomer was predominantly polymerized using *R*-**6**, while (2*R*,4*R*)-2,4-pentanediyl dimethacrylate (*RR*-**1**) enantiomer was predominantly polymerized using *S*-**6**. The obtained polymers were an optically activite, and the absolute values of the specific rotation ($[\alpha]_{435}$, *c* 0.3, in chloroform, at 28 °C) of the obtained polymers were from 18.9° to 38.6°.

Figure 1A shows the relationship between M_n, M_w/M_n, and monomer conversion for the polymerization of *rac*-**1** using the **3**/CuBr/*R*-**6** initiating system. The M_n values of the obtained polymers increased with increasing monomer conversion, and the M_w/M_n values of the obtained polymers were relatively narrow (1.21−1.28). Figure 1B shows the kinetic plots of the polymerization of *rac*-**1** using the **3**/CuBr/*R*-**6** initiating system. The apparent polymerization rates of *SS*-**1** and *RR*-**1** enantiomer were first-order with respect to the monomer concentration, indicating that the polymerization of *rac*-**1** using **3**/CuBr/*R*-**6** was living-like.

The reaction rate of the *SS*-**1** enantiomer was faster than that of the *RR*-**1** enantiomer, and the reactivity ratio of the *SS*-**1** enantiomer consumption rate ($k_{SS-\mathbf{1}}$) and the *RR*-**1** enantiomer consumption rate ($k_{RR-\mathbf{1}}$), *r* (= $k_{SS-\mathbf{1}}/k_{RR-\mathbf{1}}$), was 3.0 for **3**/CuBr/*R*-**6**. In addition, the *r* value was 1.6 for **3**/CuBr/**4**, 1.3 for **3**/CuBr/**5**, and 3.2 for **3**/CuBr/*S*-**6**. Figure 2 shows the change in *e.e.*

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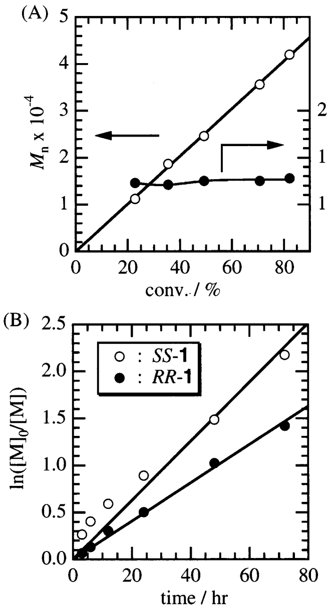


Figure 1. (A) Dependence of M_n and M_w/M_n on the monomer conversion for the polymerization of *rac*-**1** using the **3**/CuBr/*R*-**6** initiating system. (B) Kinetic plots for the polymerization of *rac*-**1** using the **3**/CuBr/*R*-**6** initiating system.

of the recovered monomer and the specific rotation of the obtained polymers as a function of monomer conversion in the polymerization of *rac*-**1** using **3**/CuBr/*R*-**6**. The *e.e.* value of the recovered monomer increased with increasing monomer conversion, but $[\alpha]_{435}$ of the resulting polymers decreased, because the optical purity (*o.p.*) of the resulting polymers decreased with increasing monomer conversion. The *o.p.* value of the resulting polymer is given by *e.e.*/conv − *e.e.*;[20] e.g., the *o.p.* values of the resulting polymer were 45.5% at 22.8% monomer conversion and 7.7% at 82.3% monomer conversion.

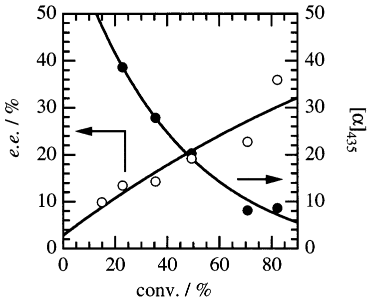
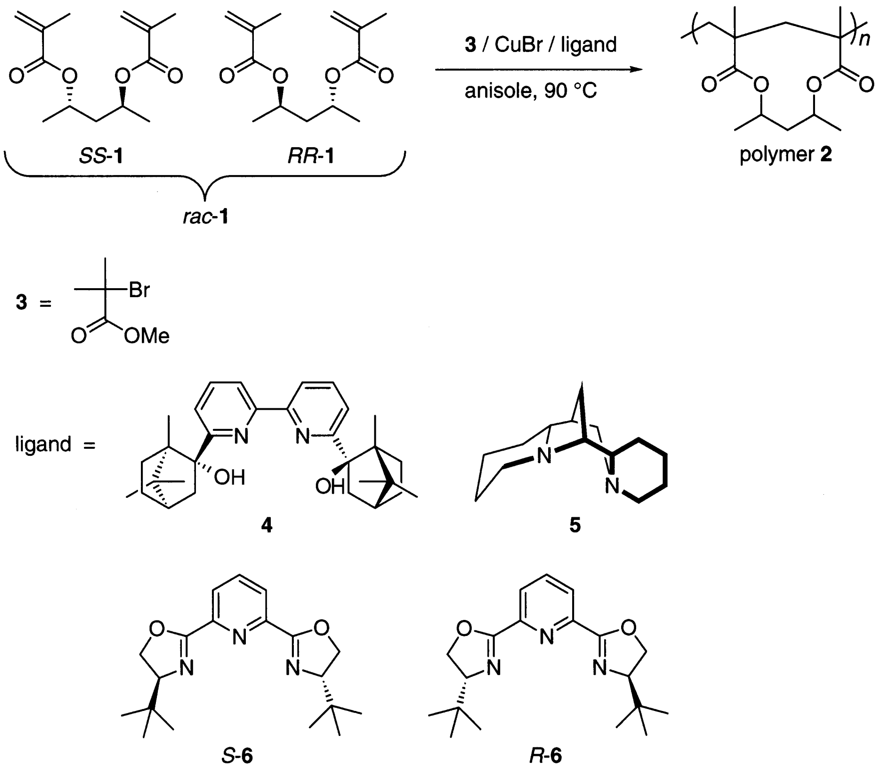


Figure 2. Relationship between *e.e.* of recovered monomer, $[\alpha]_{435}$ of polymer **2**, and monomer conversion of polymerization of *rac*-**1** using the **3**/CuBr/*R*-**6** initiating system.

This indicates that the optical activity of the polymer is due to the excess *SS*-**1** enantiomer in the obtained polymer. These results indicate that the chiral Cu complex may affect the addition of *rac*-**1** to the growing end, in which the *SS*-**1** enantiomer of *rac*-**1** was predominantly polymerized, i.e., an enantiomer-selective radical polymerization.

In summary, we achieved an enantiomer-selective polymerization by cyclopolymerizing *rac*-2,4-pentanediyl dimethacrylate (*rac*-**1**) by the atom transfer radical polymerization method using a chiral initiating system. For **3**/CuBr/*R*-**6** as the chiral initiating system, (2*S*,4*S*)-pentanediyl dimethacrylate (*SS*-**1**) was predominantly polymerized, and the enantiomeric excess (*e.e.*) of the recovered monomers increased with increasing monomer conversion, although the specific rotation of the resulting polymers decreased. To our knowledge, this is the first report describing an enantiomer-selective radical polymerization of a racemic bifunctional monomer.

Scheme 1



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(18) *rac*-2,4-Pentanediyl dimethacrylate (*rac*-**1**): Methacryloyl chloride (24.0 g, 229 mmol) was gradually added to a solution of *rac*-2,4-pentanediol (10.0 g, 96.0 mmol) in dry *N*-methyl-2-pyrrolidinone (100 mL), at 0 °C. After stirring at room temperature for 2 days, the mixture was diluted with water and then extracted with diethyl ether (100 mL × 3). The combined extracts were washed with aqueous 5% NaOH (30 mL) and water (30 mL) and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel with hexane/diethyl ether (volume ratio, 9/1) and then distilled under reduced pressure to give 14.9 g of *rac*-**1** (76.2%); bp 105 °C/0.2 mmHg. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 6.05 (s, 2H, CH_2=), 5.52 (s, 2H, CH_2=), 5.03 (m, 2H, CH), 1.92 (s, 6H, CH_3−C=), 1.88 (m, 2H, CH_2), 1.28 (d, ^2J = 6.242 Hz, CH_3, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 166.76 (C=O), 136.54 (CH_2=C), 125.08 (CH_2=), 67.78 (CH), 42.27 (CH_2), 20.40 (CH_3), 18.28 (CH_3). Anal. Calcd for $C_{13}H_{20}O_4$ (240.3): C, 64.98; H, 8.39. Found: C, 64.77; H, 8.39.

(19) Polymerization of *rac*-**1** using **3**/CuBr/**4**: In a glovebox (under moisture- and oxygen-free argon atmosphere, H_2O, $O_2 < 1$ ppm), a dry test tube was charged with *rac*-**1** (500 mg, 2.08 mmol), **3** (3.76 mg, 2.08 × 10^{-2} mmol), CuBr (5.94 mg, 4.16 × 10^{-2} mmol), **4** (38.3 mg, 8.32 × 10^{-2} mmol), and anisole (20.8 mL). A portion (2 mL) of this reaction mixture was added to separate dry test tubes, capped, and then taken out of the glovebox. The contents of the test tube were stirred at 90 °C. At the end of the polymerization, a 20 μL aliquot of the reaction mixture was added to hexane (0.5 mL) and filtered through a 0.25 μm pore membrane filter. These samples were analyzed for monomer conversion and enantiomer excess (*e.e.*) by high-performance liquid chromatography (HPLC) equipped with a CHIRALCEL OB-H column and for M_n and M_w/M_n by gel permeation chromatography (GPC). The residual polymerization mixtures were passed through a short alumina column to remove the metal salts, and the solvent was removed under reduced pressure. The residue was poured into hexane, and the precipitate was filtered. The obtained powders were purified by reprecipitation with chloroform−methanol and dried in vacuo.

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