Macromolecules **1995,** *28,* 6378–6380

(*S*)-1,3-Butanediol as a Simple Template for Asymmetric Induction in Cyclocopolymerization

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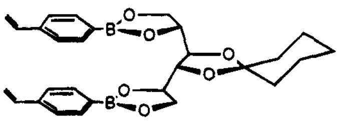
Received April 20, 1995
Revised Manuscript Received June 26, 1995

Wulff et al. have established the synthesis of the optically active vinyl polymer through cyclocopolymerization of the divinyl monomer having a chiral template with the vinyl comonomer, followed by removing the template.[1] On the basis of this cyclocopolymerization method, we recently reported that the chiral diad configuration in the polymer chain could be determined using the circular dichroism (CD) exciton chirality method.[2] During this cyclocopolymerization, the optical activity of the resulting copolymer depends on the amount of enantiomeric racemo cyclic units which form during the intramolecular cyclization.[1c] Thus, the molecular design of the monomer to form such a racemo unit is considered to be important. Wulff et al. have used 3,4-*O*-cyclohexylidene-D-mannitol 1,2:5,6-bis-*O*-[(4-vinylphenyl)borate] (**1**) in which the two (4-vinylphenyl)borate groups are arranged facing each other.[1c] On the other hand, we found the asymmetric induction using 1,4-bis(4-vinylbenzoyl)-2,3-*O*-isopropylidene-L-threitol (**2**) as the monomer without such an arrangement.[2] The structure of the monomers, **1** and **2**, is characterized by two 4-vinylphenyl groups which are connected to the chiral centers in the templates, D-mannitol and L-threitol. The relation between the asymmetric induction and the chiral requirement for the template, however, has not always been clear. For example, it is not obvious whether the compound with one asymmetric center can act as a chiral template. Here we report the synthesis of the optically active polymer using (*S*)-1,3-butanediyl bis(4-vinylbenzoate) (**3**) as the monomer having a template with one chiral center.



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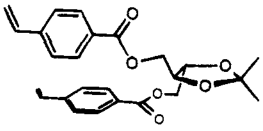

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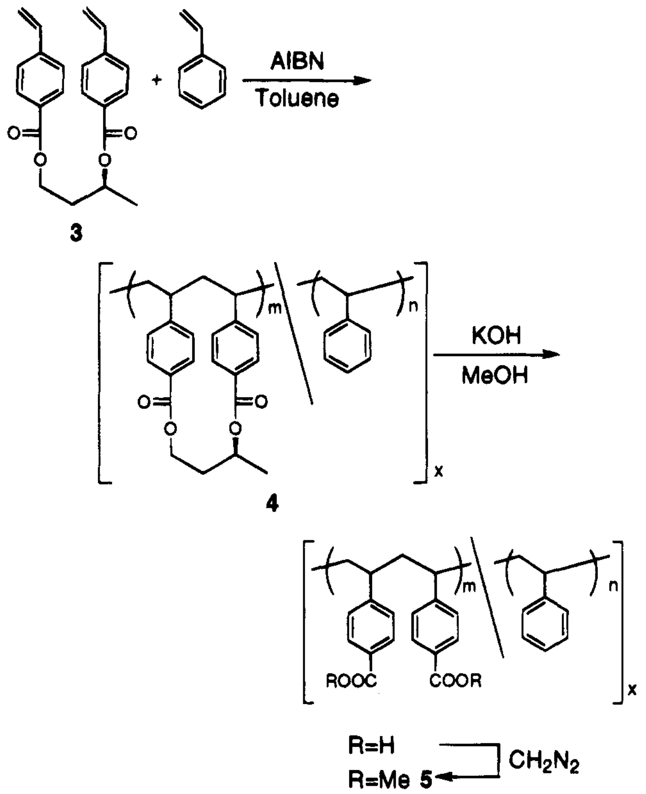
The monomer **3**, a white powder, was prepared by reacting (*S*)-1,3-butanediol with 4-vinylbenzoyl chloride.[3] The copolymerizations of **3** with styrene (St) were carried out using azobis(isobutyronitrile) (AIBN) in toluene at 60 °C.[4] Typical results are listed in Table 1. The polymerization systems were homogeneous, and the resulting copolymers (**4**) were soluble in chloroform and tetrahydrofuran. The number-average molecular weights (M_ns) of these polymers ranged from 4300 to 16 400. The characteristic absorptions at 5.3 and 5.8 ppm due to the vinyl protons disappeared in the ^{1}H-NMR spectrum of copolymer **4**. This means that the copolymers essentially consisted of the cyclic repeating and St units. The copolymerization reactivity of **3** was higher than that of St, resulting in the mole fraction of the **3** unit in copolymer **4** being higher than that in the monomer feed. The specific rotation ($[\alpha]^{23}_{435}$, *c* 1.0, CHCl$_3$) of the cyclopolymers **4** changed from +182.0° to +263.5° along with the copolymer composition.



In order to study asymmetric induction in these copolymer systems, it is necessary to quantitatively remove the chiral templates from the polymers. The removal of the chiral template from **4** was performed in aqueous MeOH using KOH, and then the hydrolyzed copolymers were treated with diazomethane to yield poly(methyl 4-vinylbenzoate-*co*-styrene) (**5**).[5] Table 1 lists the results of the synthesis of **5**. No chiral template remained in polymer **5**, because the absorption at 3.6–5.2 ppm due to the template disappeared in the ^{1}H-NMR spectrum. The obtained copolymer, i.e., poly(methyl 4-vinylbenzoate-*co*-styrene) (**5**), showed optical activity with a specific rotation ($[\alpha]^{23}_{435}$, *c* 1.0, CHCl$_3$) ranging from −4.2° to −24.0°. The sign of these values is opposite to that for **4** at every composition. This result indicated that a new chirality was induced in the main chain of the monomeric units from **3** by the twist in the (*S*)-1,3-butanediol template.

The CD exciton chirality method[6] for determining the absolute configuration of the bisbenzoate derivatives is quite suitable for analyzing the stereochemistry of monomer **3** and polymer **5**. Harada et al. applied the exciton chirality method to various chiral acyclic 1,3-glycol esters.[7] For example, the CD spectrum of (2*S*,4*S*)-2,4-pentanediyl bis(4-bromobenzoate) (**6**) first showed the positive ($\Delta\epsilon = +26.5$, 252.5 nm) and then, second, the negative ($\Delta\epsilon = -9.1$, 236.0 nm) Cotton effects. This was caused by the fact that a conformer whose pentane group takes a zigzag form in a same plane is the most preferred among its six rotational conformers. (S)-1,3-Butanediyl bis(4-bromobenzoate) (**7**), in which only one asymmetric carbon exists, also showed the splitting Cotton effect, which was positive ($\Delta\epsilon = +13.9$) at 252.6 and negative ($\Delta\epsilon = -3.9$) at 235.9 nm.

0024-9297/95/2228-6378$09.00/0

Table 1. Cyclocopolymerization of (*S*)-1,3-Butanediyl Bis(4-vinylbenzoate) (3) and Styrene (St) and Synthesis of Poly(methyl 4-vinylbenzoate-*co*-styrene) (5)

polymer 4[a]						polymer 5[b]		
mole fraction of 3 in monomer feed	time (h)	yield (%)	mole fraction of the 3 unit in copolymer[c]	M_n (M_w/M_n)[d]	$[\alpha]_{435}$[e]	yield (%)	M_n (M_w/M_n)[d]	$[\alpha]_{435}$[e]
0.7	1	16.3	0.94	16 400 (2.26)	+258.6	52.1	22 900 (1.95)	−4.2
0.5	2	20.6	0.81	13 200 (2.09)	+263.5	56.9	15 600 (1.82)	−10.3
0.3	3	18.3	0.64	8 700 (2.24)	+238.0	60.3	9 800 (2.19)	−17.0
0.1	6	11.9	0.35	4 300 (1.34)	+182.0	67.8	3 900 (1.35)	−24.0

[a] Solvent, toluene; initiator, AIBN; temp, 60 °C; [3 + St] = 0.1 mol·L^{-1}; [AIBN] = 1 g·L^{-1}. [b] Prepared from polymer 4 through hydrolysis using KOH in aqueous MeOH for 50 h under reflux and then treatment with diazomethane in benzene−ether. [c] Determined by ^{1}H NMR spectra. [d] Determined by GPC using a polystyrene standard. [e] Measured in CHCl$_3$ at 23 °C (c = 1.0).

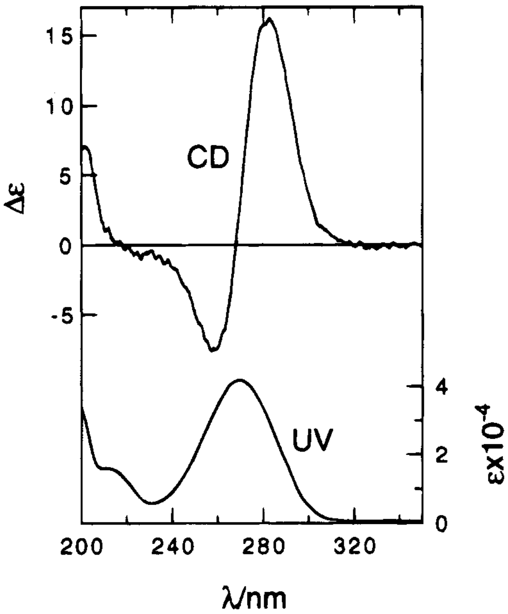


Figure 1. CD and UV spectra of monomer **3**, measured in HFP at 21 °C. The sample concentration was 0.117 mg/10 mL (3.33 × 10^{-5} mol·L^{-1}). The path length was 0.5 cm.

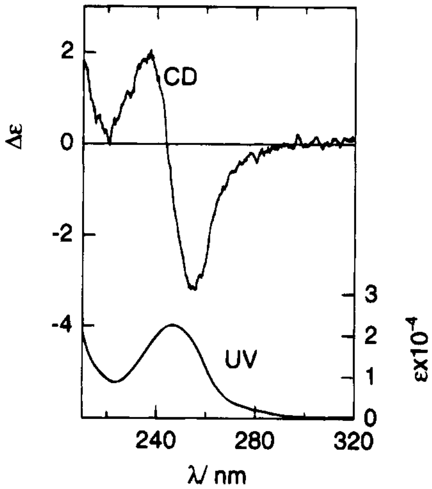


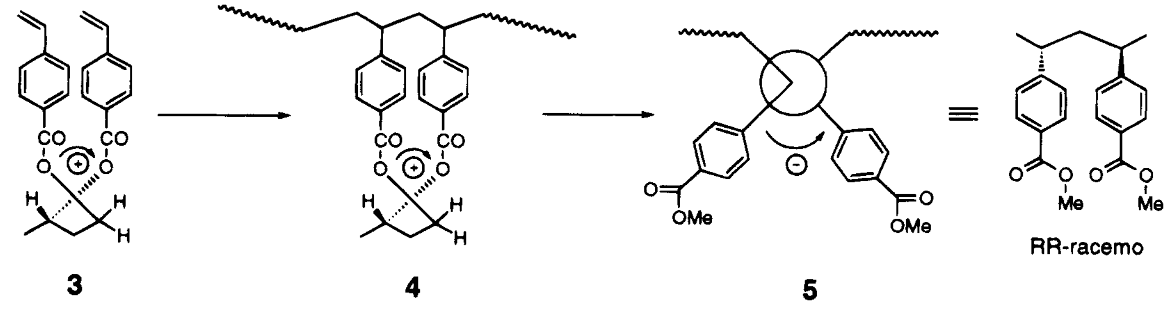
Figure 2. CD and UV spectra of polymer **5** (**3**/St = 0.35/0.65), measured in HFP at 21 °C. The sample concentration was 0.245 mg/10 mL. The Δε and ε values were based on the concentration of methyl *p*-vinylbenzoate units (4.51 × 10^{-5} mol·L^{-1}) calculated using the copolymer composition of 0.35. The path length was 0.5 cm.

Figure 1 shows the CD and UV spectra of **3**. The CD spectrum exhibits a positive Cotton effect (Δε = +16.3) at 282.7 nm and a negative one (Δε = −7.5) at 259.1 nm in the region of $\pi \rightarrow \pi^*$ transition (λ_{max} 269.6 nm). The CD spectrum in Figure 1 was similar to those of **6** and **7** except for the red shift in UV absorbance caused by the extension of the conjugated system by the vinyl groups. Consequently, monomer **3** has a positive chirality, and its benzoate chromophores, the two 4-vinylbenzoyl groups, twist clockwise as reported for **7**. This enantiotropic twist in monomer **3** is achieved by one chiral center originating from the (*S*)-1,3-butanediol which is able to act as a chiral template for the asymmetric cyclocopolymerization.

The CD spectrum of **5** (**3**/St = 0.35/0.65) showed a split Cotton effect with a negative Cotton effect at 255.2 nm and a positive one at 237.2 nm (Figure 2). Polymer **5** has a negative chirality in which two 4-vinylbenzoyl groups twist counterclockwise, resulting in an *R*,*R*-configuration of vicinal (methyl 4-vinylbenzoate) units in the main chain. Figures 1 and 2 indicate that the chirality of the dibenzoate is positive in monomer **3** but negative in polymer **5**. Such a change of chirality during the polymerization process is illustrated in Scheme 1. The (*S*)-1,3-butanediol template having one chiral center transmitted its chirality to the main chain during the intramolecular cyclization to form an enantiomeric *R*,*R*-racemo configuration in polymer **5**.

In summary, optically active poly(methyl 4-vinylbenzoate-*co*-styrene) was obtained through the radical cyclocopolymerization of (*S*)-1,3-butanediyl bis(4-vinylbenzoate) with styrene, followed by removal of the template. In previous studies,[1,2] the D-mannitol and L-threitol residues in **1** and **2** are C$_2$ symmetric, cyclic

Scheme 1. Schematic Conclusion of CD Spectrum Measurements for Asymmetric Induction during Cyclocopolymerization of 3 and St



templates with two chiral centers. For asymmetric induction during cyclocopolymerization, these stereochemical requirements have been considered to be indispensable. This study, however, shows that even an acyclic template with one chiral center such as (*S*)-1,3-butanediol was effective. This fact means that various kinds of chirality which includes chiral compounds possessing no such requirements can generally be used as a chiral template. Numerous chiral compounds have been prepared along with the progress in organic chemistry, in particular, asymmetric synthesis. The results of this investigation indicate the possibility of utilizing these widespread chiral compounds as a template for asymmetric induction during cyclocopolymerization.

Acknowledgment. This research was supported by a Research Grant from the Ministry of Education, Science, and Culture, Japan.

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(3) A solution of (*S*)-1,3-butanediol (Tokyo Kasei Kogyo Co.) (5 g, 56 mmol) in dry pyridine (200 mL) was cooled to 5 °C in an ice bath. To this solution was gradually added a solution of 4-vinylbenzoyl chloride[9] (20 g, 120 mmol) in benzene (150 mL) so that the temperature of the solution did not rise over 10 °C. The reaction mixture was stirred overnight at room temperature. The precipitate was filtered off, and the filtrate was successively washed with several portions of aqueous potassium bicarbonate and water and dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel with *n*-hexane/ether (3/2) to yield (*S*)-1,3-butanediyl bis(4-vinylbenzoate) (**3**) (13.5 g, 69%). Mp: 37 °C. $[\alpha]^{23}{}_{D} = +118.5°$, $[\alpha]^{23}{}_{435} = +283.2°$ (*c* 1.0, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$): δ 7.98 (d, J = 8.3 Hz, 2H, Ar), 7.95 (d, J = 8.6 Hz, 2H, Ar), 7.42 (d, J = 8.3 Hz, 2H, Ar), 7.40 (d, J = 8.2 Hz, 2H, Ar), 6.73 (dd, J_{trans} = 17.5 Hz, J_{cis} = 10.9 Hz, 1H, =CH−), 6.72 (dd, J_{trans} = 17.5 Hz, J_{cis} = 10.9 Hz, 1H, =CH−), 5.84 (d, J_{trans} = 17.5 Hz, 2H, $=CH_2$), 5.37 (d, J_{cis} = 10.9 Hz, 2H, $=CH_2$), 5.32−5.42 (m, 1H, CH), 4.43−4.53 (m, 2H, OCH_2), 2.11−2.27 (m, 2H, CH_2), 1.44 (s, J = 6.3 Hz, 3H, CH_3). ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 166.2, 165.7 (C=O), 141.9, 129.8, 129.6, 129.2, 126.0 (arom), 136.0 (=CH−), 116.4 (CH_2=), 68.8 (CH), 61.4 (OCH_2), 35.0 (CH_2), 20.2 (CH_3). Anal. Calcd for $C_{22}H_{22}O_4$ (350.4): C, 75.41; H, 6.33. Found: C, 75.57; H, 6.33.

(4) A typical polymerization procedure is as follows: A solution of **3** (0.779 g, 2.22 mmol), styrene (0.240 g, 2.30 mmol), and AIBN (45 mg) in dry toluene (44.0 mL) was placed in a glass ampule. This solution was degassed *in vacuo*, and gaseous N_2 was introduced. Polymerization was initiated by heating to 60 °C in a water bath. After 3 h, the polymerization mixture was poured into methanol (500 mL), and the precipitate was filtered. The obtained white powder was purified by reprecipitation with chloroform−methanol and dried *in vacuo*. Yield: 0.21 g (21%). The composition of **3** was 0.81/0.19 (*x*/*y*) which was estimated from the area ratio of aromatic and aliphatic regions in the ^1H NMR spectrum.

(5) Typical procedures for hydrolysis and methylation are as follows: To a solution of **4** (0.12 g, *x*/*y* = 0.81/0.19) in THF (4 mL) in a Teflon bottle was added 25% methanolic KOH (50 equiv to the C=O group in **4**). The reaction mixture was refluxed for 50 h along with periodically adding a small portion of water. After neutralization by 2 N hydrochloric acid with cooling in an ice bath, the mixture was transferred to a cellulose tube and dialyzed for 2 days with distilled water. The aqueous solution was freeze-dried to yield a white powder. This was added to a mixture of an ether solution (60 mL, ca. 0.5 $mol \cdot L^{-1}$) of diazomethane[9] (ca. 30 mmol) and benzene (60 mL). The polymer was dissolved with evolution of nitrogen gas. The mixture was left alone for 14 h at room temperature, and all solvents were removed under reduced pressure. The residue was dissolved in 0.5 mL of chloroform, and the solution was poured into 50 mL of methanol. The white precipitate was filtered and dried *in vacuo*. Yield: 66 mg (57%).

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MA9505484