Chirality Induction in Cyclopolymerization. 2. Synthesis of Optically Active Poly[(methyl 4-vinylbenzoate)-*co*-styrene] by Cyclocopolymerization of 1,2:5,6-Di-*O*-isopropylidene-3,4-bis-*O*-(4-vinylbenzoyl)-D-mannitol and -D-glucitol with Styrene

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ABSTRACT: 1,2:5,6-Di-*O*-isopropylidene-3,4-bis-*O*-(4-vinylbenzoyl)-D-mannitol (**1a**) and -D-glucitol (**1b**) with styrene (St) were polymerized using AIBN in toluene at 60 °C to yield copolymers (**2a** and **2b**, respectively) consisting essentially of the cyclic repeating and styrene units. In order to confirm asymmetric induction in **2**, the removal of the template from **2** was carried out using KOH in aqueous MeOH, and then the resulting hydrolyzed copolymer was treated with diazomethane for conversion into poly[(methyl 4-vinylbenzoate)-*co*-styrene] (**3**). Copolymers **2a** and **2b** showed a negative specific rotation, whereas a positive rotation was observed for **3a** and **3b**. The CD spectrum of **1a** exhibited a negative Cotton effect at 300.0 nm and a positive one at 267.3 nm as well as a negative exciton coupling of **1b**. According to the exciton chirality method, **1a** and **1b** had a negative chirality and its benzoate chromophores, the two 4-vinylbenzoyl groups, were twisted counterclockwise. On the other hand, the CD spectrum of **3a** (**1a**/St = 0.30/0.70) and **3b** (**1b**/St = 0.27/0.73) showed a split Cotton effect with a positive one at 254.9 nm and a negative one at 237.1 nm for **3a** and with a positive Cotton effect at 254.7 nm and a negative one at 232.7 nm for **3b**. This result indicated that **3** had a positive chirality in which two 4-vinylbenzoyl groups were twisted clockwise, i.e., the vicinal (methyl 4-vinylbenzoate) groups in the main chain were an (*S*,*S*)-configuration.

Introduction

The cyclocopolymerization of the divinyl monomer containing a chiral template with a monovinyl comonomer, followed by removing the template, is one certain method of synthesizing an optically active vinyl polymer.[1−6] Therefore, it is necessary to examine various chiral compounds and to determine their efficiency as a template for asymmetric induction. Carbohydrate is one of the useful sources for the cyclocopolymerization method. Wulff et al. reported the synthesis of optically active poly(4-vinylphenylboric acid-*co*-styrene) using 1,2:5,6-bis-*O*-((4-vinylphenyl)borinyl)-3,4-*O*-cyclohexylidene-D-mannitol.[1c] We reported the synthesis of optically active poly[(methyl 4-vinylbenzoate)-*co*-styrene] using bis(4-vinylbenzoate) monomers with carbohydrates, such as methyl 4,6-α-*O*-isopropylidene-D-glucopyranoside,[6] 1,2:5,6-di-*O*-isopropylidene-D-mannitol, and 2,3-*O*-isopropylidene-L-threitol.[5,6] D-Mannitol derivatives have been widely used as chiral template in organic chemistry because of their C_2 symmetric character. The C_2 symmetry has been considered to be very important in the enantioselective reaction using such a template to avoid a complexity of a face selectivity. In the asymmetric inductive polymerization, the C_2 symmetric template, such as D-mannitol and L-threitol derivatives, has been designed for the similar reason. D-Glucitol, which is an asymmetric diastereomer of D-mannitol, is commercially available. The present study aims to examine the diastereomeric effect on the chirality induction using C_2 symmetric D-mannitol and asymmetric D-glucitol templates.

In this paper, we report the radical cyclocopolymerization of 1,2:5,6-di-*O*-isopropylidene-3,4-bis-*O*-(4-vinylbenzoyl)-D-mannitol (**1a**) and -D-glucitol (**1b**) and styrene. After the alkali hydrolysis of the resulting cyclocopolymers (**2a** and **2b**, respectively), the hydrolyzed polymers were treated with diazomethane for conversion into poly[(methyl 4-vinylbenzoate)-*co*-styrene] (**3a** and **3b**, respectively) (Scheme 1). The optical activity of **3** was confirmed, and the chiroptical properties of **1** and **3** were measured. The absolute configuration of the chiral copolymers and the asymmetric induction process are discussed on the basis of the exciton chirality method.[7] In addition, the asymmetric induction using a D-glucitol template is compared with that using a D-mannitol one.

Experimental Section

Measurements. ^{1}H and ^{13}C NMR spectra were recorded using a JEOL EX-270 instrument. UV spectra were recorded on a JASCO 660 UV/vis spectrophotometer. The molecular weight of the resulting polymer was measured by gel permeation chromatography (GPC) in tetrahydrofuran on a JASCO HPLC system (PU-980 Intelligent HPLC pump and 830-RI Intelligent RI detector) equipped with three polystyrene gel columns (Shodex KF-804L). The number-average molecular weight (M_n) was calculated on the basis of polystyrene calibration. Optical rotations were determined with a JASCO DIP-140 digital polarimeter. CD spectra were measured at 21 °C in hexafluoroisopropyl alcohol (HFIP) with a 0.5 cm path length using a JASCO J-720 spectropolarimeter.

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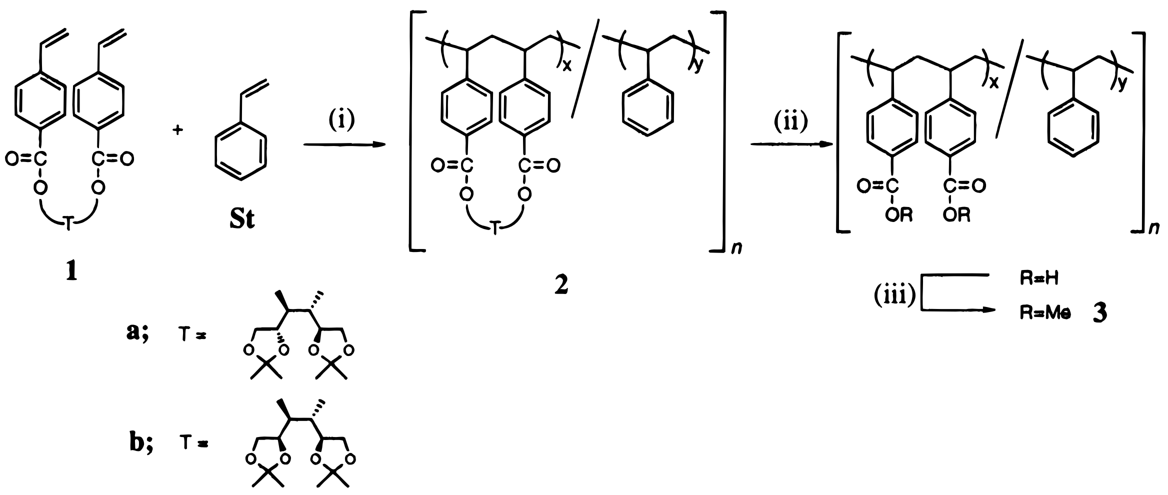
Scheme 1[a]



[a] Conditions: (i) AIBN, toluene, 60 °C; (ii) KOH, MeOH, reflux; (iii) CH_2N_2, ether, room temperature.

Table 1. Cyclocopolymerization of 1,2:5,6-Di-*O*-isopropylidene-3,4-bis-*O*-(4-vinylbenzoyl)-D-mannitol and -D-glucitol (1) with Styrene and Synthesis of Poly[(methyl 4-vinylbenzoate)-*co*-styrene] (3)[a]

monomer	f_1[c]	time, h	yield, %	F_1[d]	M_n (M_w/M_n)[e]	$[\alpha]_{435}$,[f] deg	synthesis of **3**[b] yield, %	synthesis of **3**[b] M_n (M_w/M_n)[e]	synthesis of **3**[b] $[\alpha]_{435}$,[f] deg
1a	0.10	10.8	14	0.30	7000 (1.28)	−118.7	76	7000 (1.27)	+24.0
	0.20	8.5	27	0.34	11000 (1.47)	−123.6	100	10000 (1.42)	+20.3
	0.29	5.5	28	0.44	13000 (1.65)	−113.6	60	8000 (1.63)	+17.3
	0.40	3.3	22	0.59	22000 (1.72)	−110.2	36	12000 (1.69)	+10.4
	0.48	3.8	33	0.69	22000 (2.06)	−108.2	23	9000 (1.62)	+7.6
	0.59	3.3	30	0.75	30000 (2.00)	−102.2	97	14000 (1.74)	+6.1
	0.70	2.8	32	0.81	37000 (2.13)	−102.4	63	24000 (1.99)	+4.7
	0.80	2.3	25	0.95	46000 (2.24)	−94.5	77	32000 (1.97)	+2.8
	0.90	2.0	21	0.98	52000 (2.44)	−89.4	51	38000 (1.96)	+2.8
1b	0.10	12.0	21	0.27	9000 (1.48)	−175.9	64	5000 (1.37)	+28.9
	0.20	7.75	24	0.43	13000 (1.23)	−194.4	63	7000 (1.59)	+25.9
	0.30	6.0	24	0.51	16000 (1.28)	−186.2	66	10000 (1.49)	+18.3
	0.40	4.5	26	0.61	19000 (1.37)	−175.7	65	12000 (1.69)	+13.5
	0.50	3.75	16	0.67	23000 (1.67)	−186.5	63	15000 (1.55)	+8.0
	0.60	4.0	10	0.76	27000 (1.40)	−161.7	56	15000 (1.56)	+7.4
	0.70	3.0	11	0.81	33000 (1.42)	−175.2	46	19000 (1.58)	+4.4
	0.80	1.5	15	0.92	40000 (1.60)	−169.7	53	26000 (1.63)	+2.2
	0.90	1.5	18	0.97	39000 (1.86)	−173.0	41	27000 (1.75)	0

[a] Solvent, toluene; initiator, AIBN; temperature, 60 °C; [**1** + St] = 0.1 mol·L^{-1}; [AIBN] = 6 mmol·L^{-1}. [b] Prepared from copolymer **2** through hydrolysis using KOH in aqueous MeOH for 50 h under reflux and then treatment with diazomethane in benzene−ether. [c] Mole fraction of **1** in the feed. [d] Mole fraction of **1** unit in copolymer **3**, determined by ^{1}H NMR spectrum. [e] Determined by GPC using a polystyrene standard. [f] Measured in $CHCl_3$ at 23 °C (c = 1.0).

Materials. 1,2:5,6-Di-*O*-isopropylidene-D-glucitol was prepared by the reported procedure.[8] The procedure for the synthesis of 1,2:5,6-di-*O*-isopropylidene-3,4-bis-*O*-(4-vinylbenzoyl)-D-glucitol (**1a**) was described before.[6] Toluene and benzene were refluxed over sodium benzophenone ketyl and distilled just before use. Pyridine was distilled from CaH_2. α,α′-Azobisisobutyronitrile (AIBN) was recrystallized from methanol. Hexafluoroisopropyl alcohol was given by Central Glass Co. and used without further purification.

1,2:5,6-Di-*O*-isopropylidene-3,4-bis-*O*-(4-vinylbenzoyl)-D-glucitol (1b). A solution of 1,2:5,6-di-*O*-isopropylidene-D-glucitol (6.6 g, 0.025 mol) in pyridine (160 mL) was cooled to 5 °C. 4-Vinylbenzoyl chloride (9.2 g, 0.055 mol) was added dropwise over a 30-min period. The mixture was heated to 80 °C and stirred for 4 h. After the mixture was cooled to room temperature, 130 mL of water was added and the resulting red-brown solution was stirred for 1 h. The solution was extracted with three portions of 75 mL of $CHCl_3$, and the extract was washed successively with three portions of 100 mL of 0.1 N aqueous HCl, 5% (w/w) aqueous NaOH, and water. The organic layer was dried over Na_2SO_4 and evaporated *in vacuo* to dryness. Flash column chromatography using silica gel (Kiesel Gel 60) with ethyl acetate/*n*-hexane (2/7, v/v) gave **1b** as a white powder. This material was stored as a solution in toluene. Yield: 11 g (0.021 mol, 84%). Specific rotation: $[\alpha]^{23}_{D} = +56.3$, $[\alpha]^{23}_{577} = +58.9$, $[\alpha]^{23}_{546} = +69.0$, $[\alpha]^{23}_{435} = +121.3$, $[\alpha]^{23}_{405} = +147.6$ (c 1.0, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$): δ (ppm) 8.02 (dd, ^3J = 8.6 Hz, 4H, Ar), 7.46 (dd, ^3J = 8.3 Hz, 4H, Ar), 6.74 (dd, $^3J_{trans}$ = 17.6 Hz, $^3J_{cis}$ = 10.6 Hz, 2H, =CH−), 5.86 (dd, $^3J_{trans}$ = 17.6 Hz, 2H, =CH_2), 5.56−5.90 (m, 2H, C^3H and C^4H), 5.39 (dd, $^3J_{cis}$ = 10.9 Hz, 2H, =CH_2), 4.40 (q, ^3J = 5.7 Hz, C^2H and C^5H), 3.91−4.15 (m, 4H, C^1H_2 and C^6H_2), 1.39 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.27 (s, 3H, CH_3). ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 165.4 (C=O), 142.3, 130.2, 130.1, 128.5, 126.2 (Ar), 135.9 (=CH−), 116.8, 116.7 (CH_2=), 109.9, 109.5 (C), 74.8, 74.6 (CH), 71.9, 71.6 (CH), 65.8, 65.6 (CH_2), 26.4, 26.2, 25.2, 25.1 (CH_3). IR (KBr): ν (cm^{-1}) 1723 (C=O, st), 1606 (C=C, st). Anal. Calcd for $C_{30}H_{34}O_8$ (522.6): C, 68.95; H, 6.21. Found: C, 68.76; H, 6.58.

Cyclocopolymerization. The copolymerization of **1** and styrene was carried out using AIBN in toluene at 60 °C. After an appropriate time, the polymerization mixture was poured into methanol and the precipitate was filtered. The obtained polymer was purified by reprecipitation with chloroform−methanol and dried *in vacuo*. The composition of **2** was determined from the area of aromatic (6−8 ppm) and alkoxy (3.5−5.5 ppm) regions in the ^{1}H NMR spectrum.

Synthesis of Poly[(methyl 4-vinylbenzoate)-*co*-styrene] (3). The procedures were reported in previous papers.[5,6]

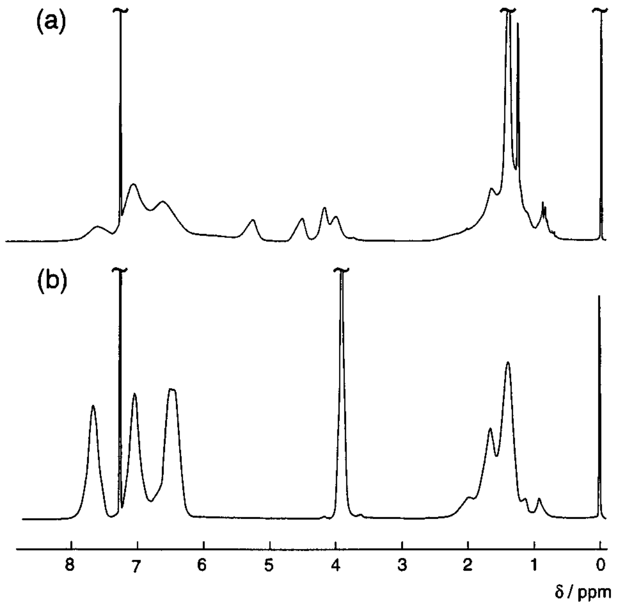


Figure 1. ^{1}H NMR spectra (270 MHz) of (a) polymer **2a** (x/y = 0.30/0.70) and (b) polymer **3a** (x/y = 0.30/0.70) measured in $CDCl_3$ using TMS as a reference.

The removal of the chiral template from **2** was carried out using KOH in aqueous MeOH, and then the hydrolyzed copolymers were treated with diazomethane in benzene/ether.

Results and Discussion

Table 1 lists the results of the copolymerizations of **1a** and **1b** with styrene (St) which were carried out using AIBN in toluene at 60 °C. The polymerization systems were homogeneous, and the resulting copolymers (**2a** and **2b**) were soluble in chloroform and tetrahydrofuran. The number-average molecular weights (M_ns) of these polymers increased with increasing St units changed from 7000 to 52 000 for **2a** and from 9000 to 40 000 for **2b**. The characteristic absorption at 5.3 and 5.8 ppm due to the vinyl protons disappeared in the ^{1}H-NMR spectrum of copolymer **2a** (Figure 1). This means that the copolymers consisted essentially of the cyclic repeating and St units. The monomer reactive ratio was $r_1 = 2.37$ and $r_{St} = 0.54$ for **1a** and $r_1 = 2.16$ and $r_{St} = 0.32$ for **1b**, resulting in the mole fraction of **1** unit in the copolymer **2** being higher than that in the monomer feed. The results indicate that the diastereomeric structure, D-mannitol and D-glucitol, did not apparently affect the cyclization tendency and copolymerization reactivity.

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 D-mannitol and D-glucitol templates from **2** was carried out using KOH in aqueous MeOH, and then the hydrolyzed copolymer was treated with diazomethane for conversion to the methylated polymer. The absence of the template in the resulting polymer was confirmed by the disappearance of the absorption at 3.6−5.2 ppm due to the template in the ^{1}H-NMR spectrum (Figure 1). Table 1 lists the results of the synthesis of methylated copolymers, i.e., poly(methyl 4-vinylbenzoate-*co*-styrene) (**3a** and **3b**).

The specific rotation ($[\alpha]_{435}$, c 1.0, $CHCl_3$) of the cyclopolymers changed from −89.4° to −123.6° for **2a** and from −161.7° to −194.4° for **2b** along with the copolymer composition, while the template-free polymers also showed optical activity with a specific rotation ranging from +2.8° to +24.0° for **3a** and from +2.2° to +28.9° for **3b**. The rotatory powers due to the **1** units in polymers **2** and **3** were estimated from the specific rotations of the polymers divided by the weight fraction of the **1** units ($[\alpha]/W_1$), as shown in Figures 2 and 3. For both **2** and **3**, and absolute value of the $[\alpha]/W_1$ increased with an increase in St units in the copolymer composition. The value was 142.4° for **2a** (x/y = 0.44/0.56), 24.4° for **3a** (x/y = 0.44/0.56), 243.0° for **2b** (x/y = 0.43/0.57), and 36.9° for **3b** (x/y = 0.43/0.57). This result means that asymmetric induction increases with the decreasing sequence of **1** units. The sign of the values for **3** is opposite to that for **2** at every composition, indicating that a new chirality is induced in the main chain of monomeric units due to **1** by the asymmetry of the templates.

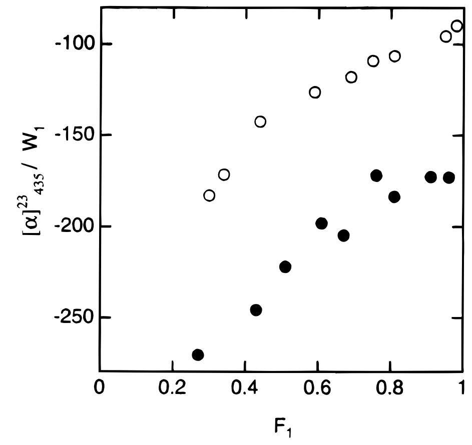


Figure 2. Specific rotations ($[\alpha]^{23}_{435}$, c = 1.0 in $CHCl_3$) of copolymer **2a** (○) and **2b** (●) divided by the weight fraction of **1** units (w_1) versus mole fraction of monomer units in copolymer.

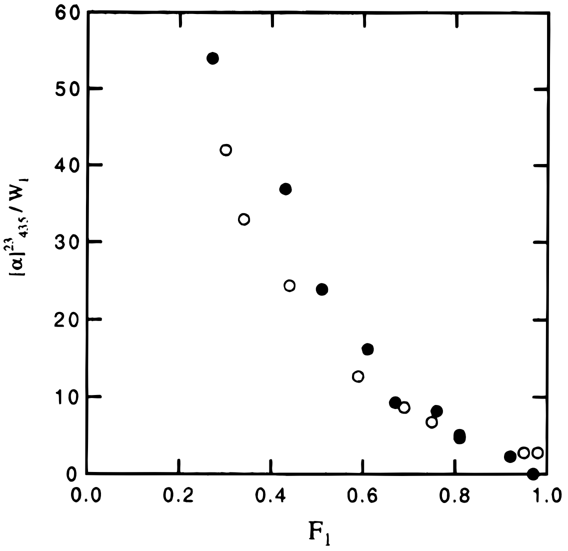
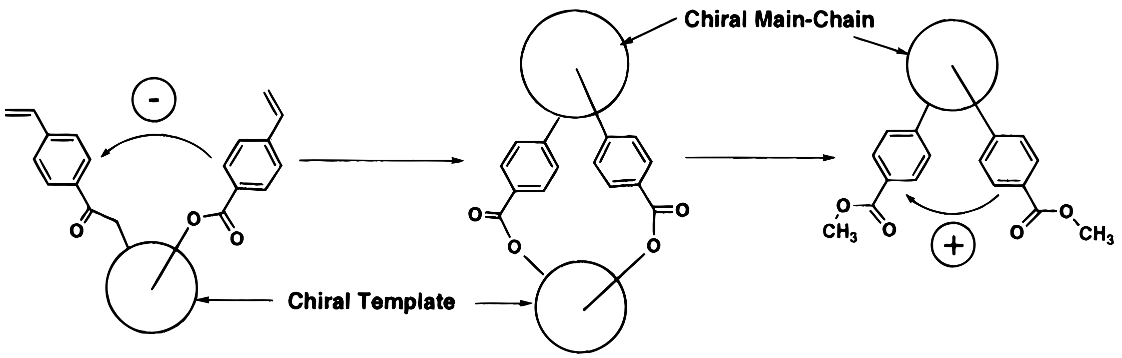


Figure 3. Specific rotations ($[\alpha]^{23}_{435}$, c = 1.0 in $CHCl_3$) of copolymer **3a** (○) and **3b** (●) divided by the weight fraction of bis(methyl 4-vinylbenzoate) units (w_1) versus mole fraction of bis(methyl 4-vinylbenzoate) units in copolymer.

The CD exciton chirality method for determining the absolute configuration of the dibenzoate of diols can be applied for analyzing the stereochemistry of monomers **1** and polymers **3**. Figure 4 shows the CD and UV spectra of **1a** and **1b**. The CD spectrum of **1a** exhibits a split Cotton effect with $\Delta\epsilon = -2.6$ at 300.0 nm and $\Delta\epsilon = +8.2$ at 267.3 nm in the region of $\pi \rightarrow \pi^*$ transition (λ_{max} 274.1 nm). Similarly, the monomer **1b** showed a

Scheme 2



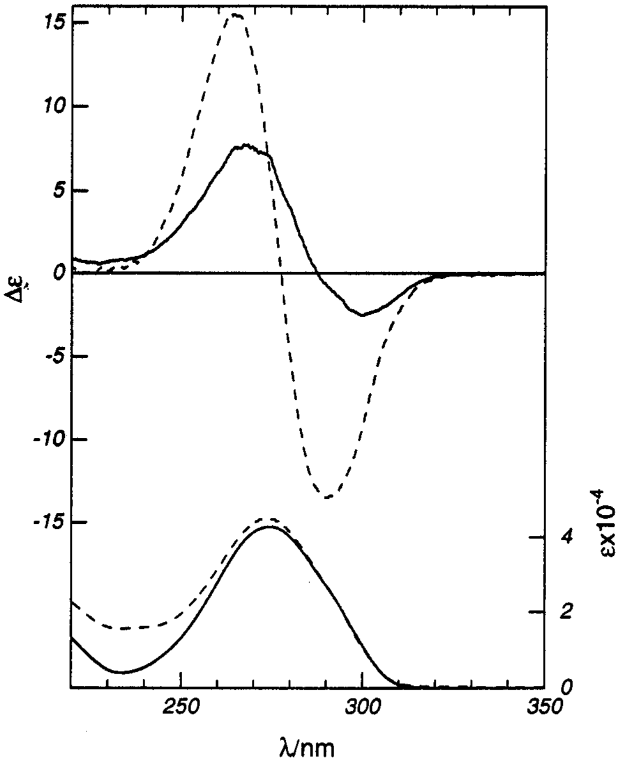


Figure 4. CD (upper) and UV (lower) spectra of monomer **1a** (- - -) and **1b** (—), recorded in HFIP at 21 °C using a path length of 5 mm.

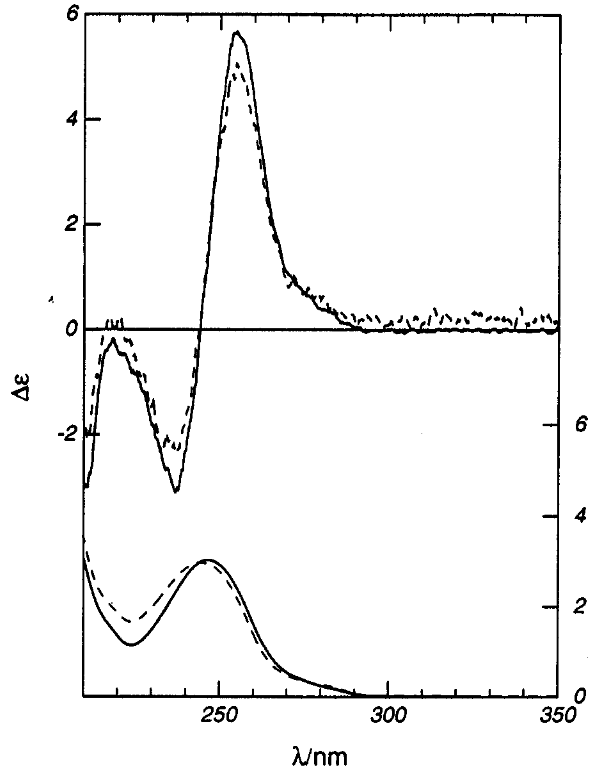


Figure 5. CD (upper) and UV (lower) spectra of copolymer **3a** (- - -, $x/y = 0.30/0.70$) and **1b** (—, $x/y = 0.27/0.73$), recorded in HFIP at 21 °C using a path length of 5 mm.

negative exciton coupling with a negative Cotton effect ($\Delta\epsilon = -13.5$) at 289.4 nm and a positive one ($\Delta\epsilon = +15.6$) at 263.4 nm in the region of UV absorption (λ_{max} 274.1 nm). Monomers **1a** and **1b** have a negative chirality, and their benzoate chromophores, the two 4-vinylbenzoyl groups, twist counterclockwise. On the other hand, the CD spectrum of **3a** ($x/y = 0.30/0.70$) shows a positive exciton coupling ($\Delta\epsilon = +5.66$ at 254.9 nm and $\Delta\epsilon = -3.10$ at 236.7 nm) as well as that of **3b** with ($\Delta\epsilon = +5.08$ at 254.7 nm $\Delta\epsilon = -2.35$ at 238.1 nm) (Figure 5). This means that polymers **3** has a positive chirality in which two 4-vinylbenzoyl groups twist clockwise, i.e., the vicinal (methyl 4-vinylbenzoate) groups in the main chain are an (*S*,*S*)-configuration. Figures 4 and 5 indicate that the negative chirality of the dibenzoate in monomer **1** changes to the positive one in polymer **3**. The configurational change in the polymerization process is shown in Scheme 2. The D-mannitol and D-glucitol templates transmitted their chirality to the main chain during the intramolecular cyclization to form an enantiomeric *S*,*S*-racemo configuration in both polymer **3**.

Because the copolymerization profiles of the monomers **1a** and **1b** are similar, the asymmetric induction can be comparable simply by the CD spectra and/or the specific rotations at the same composition. The asymmetric induction in poly[(methyl 4-vinylbenzoate)-*co*-styrene] for **1a** was lower than that for **1b**, as shown in Figure 3. D-Mannitol and D-glucitol are diastereomers of hexitols in which the former is C_2 symmetric and the latter asymmetric. Therefore, the CD spectrum of **1a** was apparently different from that of **1b**, so that the stereochemical circumstances of the two 4-vinylbenzoates at the 3,4-positions should be unequal between **1a** and **1b**. Nakanishi et al. reported that for the exciton coupling of two chromophores the maximum wavelength (λ_{max}) of the UV spectrum depends on the dihedral angle between the two benzoate groups. The value of λ_{max} for **1a** is 274.1 nm, which differs from that of 263.4 nm for **1b**. This means that the dihedral angle between the two 4-vinylbenzoate groups for **1b** is larger than that for **1a**. In addition, the *A* value, the CD amplitude of exciton Cotton effects, is inversely proportional to the square of the distance between two chromophores.[7] The *A* value is -29.1 for **1b**, which is three times that of −10.8 for **1a**. Therefore, the distance between the two 4-vinylbenzoates for **1a** is estimated to be approximately 1.7 times as long as that for **1b**. The differences in the chiral twist structure between **1a** and **1b** should be the cause of the different efficiency of asymmetric induction in the polymerization process.

Concluding Remarks

Optically active poly[(methyl 4-vinylbenzoate)-*co*-styrene] (**3**) was obtained through the radical cyclocopolymerization of both 1,2:5,6-di-*O*-isopropylidene-3,4-bis-*O*-(4-vinylbenzoyl)-D-mannitol (**1a**) and -D-glucitol (**1b**) and styrene, followed by removing the template. According to the exciton chirality method, monomer **1** and polymer **3** had a negative and a positive chirality, respectively. The templates in monomer **1** transmitted its chirality to the main chain during the intramolecular cyclization to form an enantiomeric *S*,*S*-racemo configuration in both polymers **3a** and **3b**. For the asymmetric induction based on the cyclocopolymerization method, the C_1 D-glucitol template was more efficient than the C_2 symmetric D-mannitol one.

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