Photocontrolled Chiral Recognition by [4-(Phenylazo)phenyl]carbamoylated Cellulose and Amylose Membranes

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ABSTRACT: Cellulose and amylose derivatives bearing a photoresponsive [4-(phenylazo)phenyl]carbamate residue incorporated at the 2,3,6-, 6-, or 2,3-positions of the glucose units were prepared. Enantioselective adsorption of several neutral racemates on the solid derivative membranes was investigated during the course of *trans–cis* isomerization of the pendant azobenzene residues. The chiral recognition ability was influenced by the *trans* or *cis* content, and the *trans* isomers of the polysaccharide derivatives showed higher enantioselectivity than the *cis* isomers. The difference in chiral recognition of these polymers was discussed on the basis of CD and ^{1}H NMR spectroscopic data and a molecular modeling study. In addition to the enantioselectivity, the solubility of the polysaccharide derivatives was also controlled reversibly by photoisomerization of the pendant azobenzene moieties.

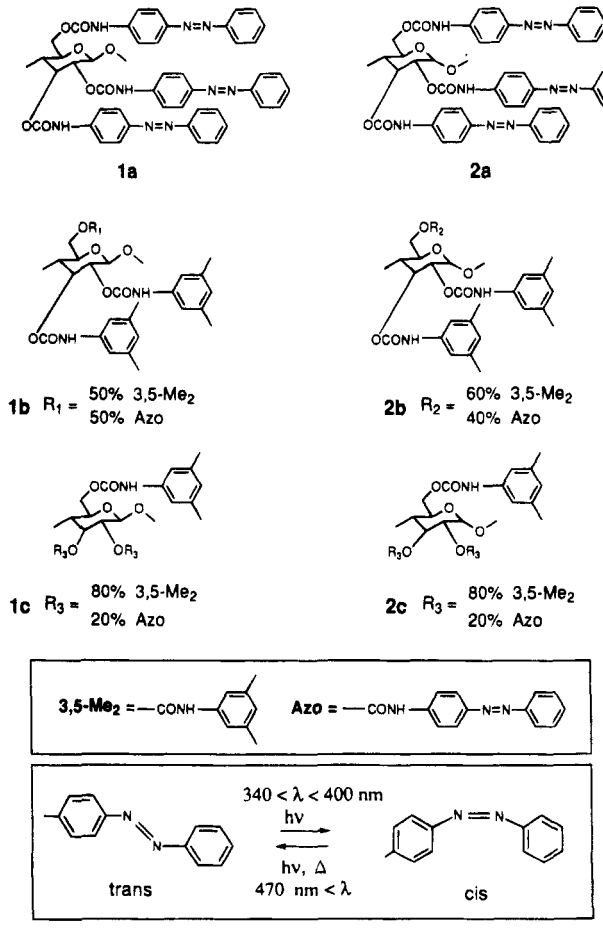
Introduction

Development of photoswitchable devices has attracted much attention. Photocontrol of physical and chemical properties[1] such as viscosity,[2] volume,[3] permeability,[4] solubility,[5] conformation,[6] catalytic activity,[7] and phase separation[8] has recently been performed with photochromic polymers. The binding abilities of azobenzene-capped cyclodextrins[9] to organic substrates and azobenzene-modified crown ethers[10] to metal ions are also photocontrolled in an on–off fashion. However, photocontrol of chiral recognition has not yet been generalized except for one example, where a chiral azobenzene-capped β-cyclodextrin was used to regulate the binding of enantiomers during *trans–cis* photoisomerization.[11]

Previously, we prepared cellulose tris[[4-(phenylazo)-phenyl]carbamate] having photoresponsive pendant groups and demonstrated that the cellulose derivative showed different chiral recognition abilities depending on the content of the *cis* structure of azobenzene pendant groups when it was used as a chiral stationary phase (CSP) in high-performance liquid chromatography (HPLC).[12] We also reported that phenylcarbamate derivatives of cellulose and amylose show a high resolving power as CSPs and can resolve a wide range of racemates.[13] Especially, cellulose tris[(3,5-dimethylphenyl)carbamate] is one of the most eligible CSPs for many racemates.[14] A solid polymer membrane of this polymer was recently found to show a high enantioselective adsorption power to some racemates and can efficiently enrich enantiomers of a drug, oxprenolol, through permeation.[15] These results led us to prepare the photoresponsive polysaccharide membranes bearing [4-(phenylazo)phenyl] carbamate residues whose chiral recognition ability such as the enantioselective adsorption ability may be controlled using light as a trigger.

In the present study, we prepared a series of phenylcarbamoylated polysaccharides having a [4-(phenylazo)-phenyl]carbamoyl group as a photoresponsive side group (Chart 1). Besides the tris[[4-(phenylazo)phenyl]carbamate]s of cellulose (**1a**) and amylose (**2a**), two regioselectively carbamoylated derivatives with [4-(phenylazo)-phenyl] and (3,5-dimethylphenyl)carbamoyl residues

Chart 1



were prepared. One has the [4-(phenylazo)phenyl]-carbamoyl group at part of the 6-position and the (3,5-dimethylphenyl)carbamoyl group at the remaining part of the 6-position and the 2- and 3-positions of a glucose unit in cellulose (**1b**) and amylose (**2b**); the other has the [4-(phenylazo)phenyl]carbamoyl group at part of the 2- and 3-positions and the (3,5-dimethylphenyl)carbamoyl group at the remaining part of the 2- and 3-positions and the 6-position of the cellulose (**1c**) and amylose (**2c**). Properties and the enantioselective adsorption ability

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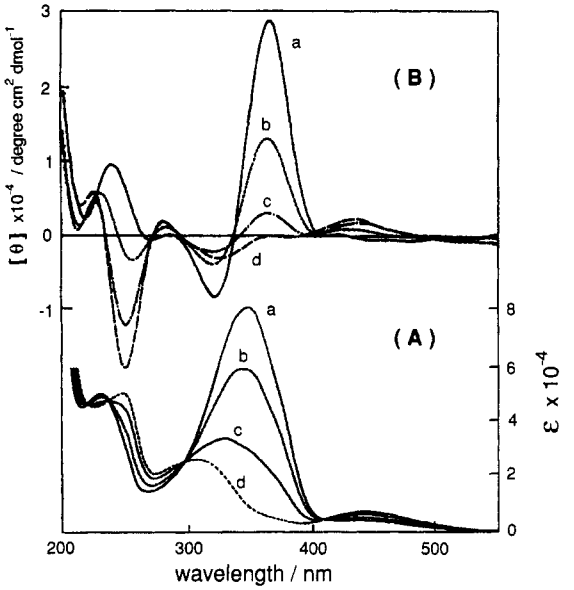


Figure 1. Absorption (A) and CD (B) spectra during the *trans*–*cis* isomerization of **1a** in THF (*trans* content; (a) 100, (b) 70, (c) 30, (d) 0%).

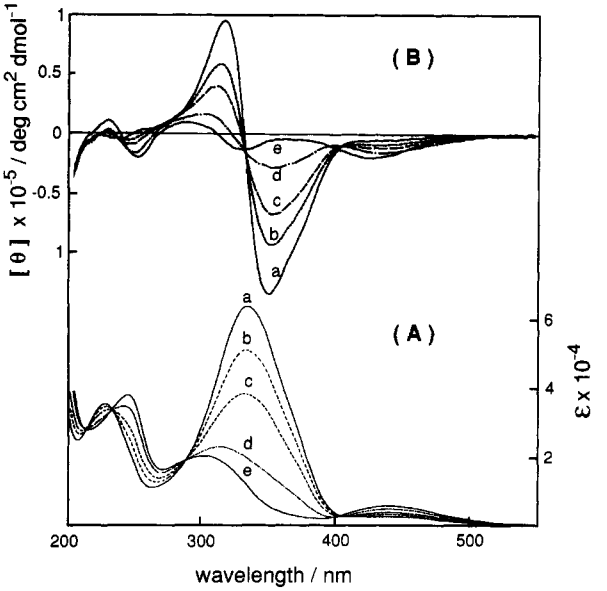


Figure 2. Absorption (A) and CD (B) spectra during the *trans*–*cis* isomerization of **2a** in THF (*trans* content; (a) 100, (b) 75, (c) 55, (d) 20, (e) 0%).

of the chiral membranes of the phenylcarbamates were investigated in order to realize photocontrol of chiral recognition.

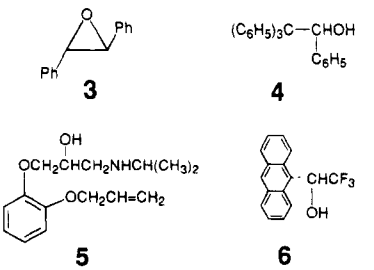
Results and Discussion

Synthesis and Photoisomerization. Tris[[4-(phenylazo)phenyl]carbamate]s of cellulose (**1a**) and amylose (**2a**) were prepared by the reaction of an excess of 4-(phenylazo)phenyl isocyanate with cellulose and amylose, respectively, in dry pyridine according to the previously reported method.[12] The regioselectively [4-(phenylazo)phenyl]carbamoylated cellulose and amylose were prepared according to the previously reported method[16] using 6-*O*-(triphenylmethyl)cellulose and amylose as the starting material. These products were identified by ^{1}H NMR spectroscopy and elemental analysis. The contents of the 4-(phenylazo)phenyl moieties are shown in Chart 1 (see also Experimental Section).

Figures 1 and 2 show the changes in the absorption and CD spectra of **1a** and **2a** in a THF solution during the course of photoisomerization, respectively. When a solution of **1a** was irradiated by light (340–400 nm), an intense absorption band at 346 nm due to the π–π^* transition of the *trans* form of pendant azobenzene residues decreased and shifted to shorter wavelengths, while an absorption at around 443 nm due to the n–π^* transition of the *cis* form increased. These changes were completely reversible, and the spectra apparently had four isosbestic points. These results indicate that no side reaction such as degradation occurred during the *trans*–*cis* photoisomerization. The changes in the absorption spectra were similar to those observed for the model compound, methyl [4-(phenylazo)phenyl]-carbamate, which showed absorption maxima at 355 and 444 nm for the *trans* and *cis* forms, respectively.[12] Similar absorption spectral changes were also observed for **2a** in THF (Figure 2). The CD spectra of *trans*-**1a** in THF exhibited an intense induced band at 367 nm, probably due to regularly arranged *trans*-azobenzene units. The intensity of this peak decreased with an increase in the *cis* content, and almost no peak was found in this region for the *cis* isomer, while the intensity at 436 nm due to the *cis*-azobenzene residues increased with an increase in the *cis* content. The *trans*-form of **1a** had a positive CD peak at around 250 nm. Its pattern markedly changed, accompanying an inversion of the sign of [θ]. These changes may arise from a conformational change in the polymer backbone due to irrardiation. The changes in the CD were also reversible. *trans*-**2a** gave an intense induced CD at around 300–400 nm in THF with a negative exciton coupling band. The intensity and pattern of **2a** differ from those of **1a**. The magnitude of CD of **2a** was more intense than those of **1a** and decreased with an increase in the *cis* content, as seen in the case of **1a**. The CD pattern at around 250 nm also changed during the isomerization. These changes were also reversible.

The absorption and CD spectra of other polymers (**b** and **c**) in THF also changed reversibly during the isomerization (figures in supporting information). However, the CD spectra below 250 nm did not exhibit a significant change during the isomerization. Probably, the content of the azobenzene moieties incorporated into the polymers (**b** and **c**) was not enough for inducing a conformational change in the polymer backbone.

Enantioselective Adsorption. The results of enantioselective adsorption of racemates **3**–**5** on the *trans*, *cis*, and *cis*-to-*trans* membranes of **1a** and **2a** are summarized in Table 1. The *cis* membranes were prepared by casting a THF solution of the *cis* isomers.



The *cis* contents of the *cis* films were estimated from the absorption spectra of the polysaccharide derivatives in THF recovered from the *cis* films just after the enantioselective-adsorption experiments on the *cis* films.[17] The % ee was dependent on the kind of analytes. The

Table 1. Enantioselective Adsorption of 1a and 2a Membranes[a]

	1a						2a					
	trans[b]		*cis*[c]		*cis*-to-*trans*[d]		*trans*[b]		*cis*[c]		*cis*-to-*trans*[d]	
racemate	% ee[e]	amt[f] (wt %)	% ee[e]	amt[f] (wt %)	% ee[e]	amt[f] (wt %)	% ee[e]	amt[f] (wt %)	% ee[e]	amt[f] (wt %)	% ee[e]	amt[f] (wt %)
3	23.7 (−)	0.8	9.4 (−)	0.6	23.0 (−)	0.9	32.6 (−)	0.9	6.4 (−)	0.5	8.6 (−)	0.7
4	13.8 (−)	1.1	3.6 (−)	0.5	9.5 (−)	1.3	39.3 (−)	3.2	13.8 (−)	0.9	20.8 (−)	1.7
5	7.4 (−)	1.3	8.3 (−)	0.8	11.8 (−)	1.5						

[a] Average values of several independent runs. [b] The membrane was prepared by casting a THF solution of the *trans* isomer. [c] The membrane was prepared by casting a THF solution of the *cis* isomer (*cis* content: 65−75%). [d] The membrane prepared by casting a THF solution of the *cis* isomer was isomerized to the *trans* form. [e] The enantioselectivities were reproducible in about ±4% ee on repeated runs. In parentheses is shown the sign of optical rotation of the enantiomer preferentially adsorbed on the membranes. [f] The amount of analytes adsorbed on the polymer.

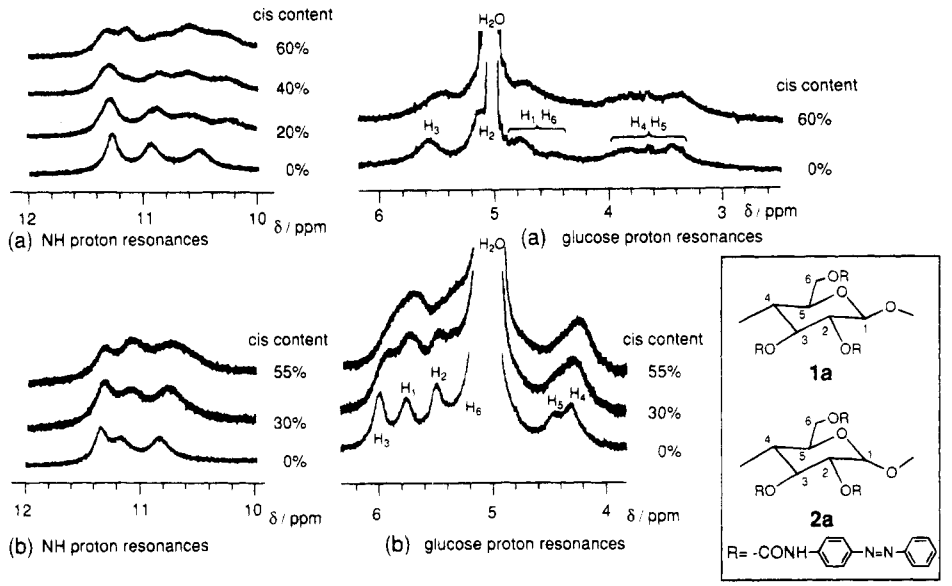


Figure 3. Change of ^{1}H NMR spectra during the *cis*−*trans* isomerization of **1a** (a) and **2a** (b) (pyridine-d_5, 20 °C, 500 MHz). Assignments were made on the basis of 2D COSY spectra of the *trans* form. The *cis* content was estimated on the basis of the absorption spectra of the same sample.

trans membrane of **1a** showed a higher enantioselective adsorption power than the *cis* membrane for analytes **3** and **4**. A similar higher enantioselectivity of *trans*-**1a** than that of *cis*-**1a** was observed when **1a** was used as a CSP for HPLC; *trans*-**1a** showed an efficient resolution of some enantiomers, while *cis*-**1a** showed poor resolution.[12] The *cis*-to-*trans* membrane of **1a** prepared from the *cis* membrane by isomerization showed almost the same enantioselectivity as the original *trans* membrane for **3**, whereas the membrane showed a lower enantioselectivity for **4** than the original *trans* membrane. Analyte **5** was absorbed on the *cis*-to-*trans* membrane in a higher ee than on the *trans* membrane.

The *trans* membrane **2a** showed a much higher enantioselective adsorption power than the *cis* membrane. The % ee of the analytes adsorbed on the *cis* membrane was increased when the *cis* membrane was isomerized to the *trans* membranes, although the membrane showed lower chiral recognition than the original *trans* membrane.

To gain insight into the conformational change in these polymers during the isomerization, the change of ^{1}H-NMR spectra of **1a** and **2a** was followed (Figure 3). A remarkable change was observed in the NH proton resonances of the carbamate residues (lower field) and glucose unit proton resonances (higher field). This indicates that the conformation of the main chain glucose units as well as the carbamoyl side groups may be changed by the isomerization in solution. Especially, the change in the resonances of the main chain of **2a** was pronounced and this must correlate to the different enantioselectivity between *trans*- and *cis*-**2a**.

In the solid state, the azobenzene residues also altered their structure during the isomerization. However, photoisomerization of *trans*-**1a** and **2a** films to the *cis* forms did not proceed completely; the maximum *cis* content is *ca.* 55% for **1a** and **2a** and *ca.* 80% for **1b**, **1c**, **2b**, and **2c** films, although photoisomerization and thermal isomerization of *cis* films to the *trans* forms proceeded completely.[17] Figure 4 shows typical CD spectra of the *trans*, *cis*, and *cis*-to-*trans* films of **2a**. The films showed Cotton effects different from those in solution, and the *trans* film showed a very intense CD in the region of 300−450 nm, while the *cis* film showed a weak induced CD. Probably, *cis*-**2a** may not take a regular orientation of the pendant azobenzene residues because of the bent structure. The *cis*-to-*trans* film obtained by the isomerization of the *cis* film showed a weak CD with different peak top wavelengths and intensities compared with those of the original *trans* film. In these *trans* films, the azobenzene residues may have different orientations. The spectral pattern and intensity were scarcely changed by rotating the sample cast on a quartz plate by 90, 180, and 270° from the first position around the axis of the incident light beam. The isomerization may influence not only the structure but also the orientation of the side groups even in the solid state. A similar spectral change in the CD was also observed in the **1a** film during the *trans*−*cis* isomerization. However, the *trans* and *cis* films of the

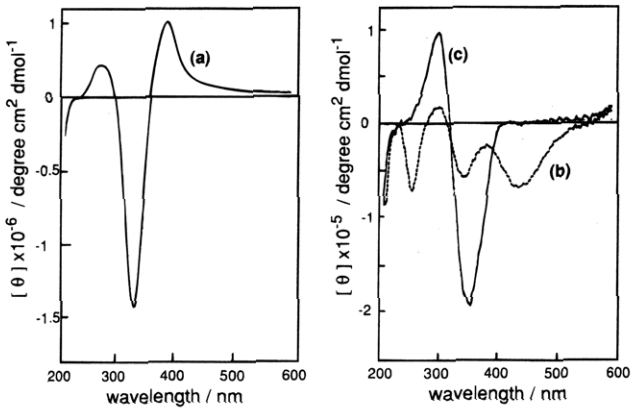


Figure 4. CD spectra of **2a** films prepared by casting a THF solution of the *trans* isomer (a) and *cis* isomer (b). The CD spectrum of the *trans* film isomerized from the *cis* film is also shown in (c) (*trans* content; (a) 100, (b) 5, (c) 95%).

other polymers **1b**, **1c**, **2b**, and **2c** exhibited weak induced CD peaks and their spectral patterns were not significantly different from each other in the 300–500 nm range during the *trans–cis* isomerization.

The difference in the chiral recognition abilities of the membranes (**1a** and **2a**) may be due to different higher-order structures of the polymers in the solid state. Because the *trans* film shows a very intense induced CD compared with the *cis* films, the polymers in the *trans* form may take a higher-order structure with a regular arrangement of the side groups. These differences must affect the chiral recognition ability of the polymers. The polymers with the *cis* form may exist in a disordered structure.

It has been reported that tris(phenylcarbamate)s of cellulose and amylose likely possess the conformations of left-handed 3-fold (3/2) and 4-fold (4/1) helices, respectively, on the basis of X-ray analysis.[18,19] The derivatives **1a** and **2a** may have similar conformations. The intramolecular hydrogen bond along the polysaccharide backbone may participate in the formation of the rigid conformations.[18,19] Such regular-ordered structures appear possible only for the *trans* isomers. The most important adsorbing sites on phenylcarbamates of cellulose and amylose as CSPs have been considered to be polar carbamate residues, which can interact with racemates mainly through hydrogen bonding in nonpolar eluent systems such as hexane–2-propanol mixtures.[13–16] Recent NMR in $CDCl_3$ and computational studies on chiral discrimination of cellulose phenylcarbamate derivatives support the mechanism.[20,21] Figure 5 shows the calculated structures of *trans*- and *cis*-**1a** optimized by a molecular mechanics calculation based on the reported structure of cellulose tris(phenylcarbamate).[18] The pendant [4-(phenylazo)phenyl]carbamate residues were arranged regularly in *trans*-**1a**, while those of *cis*-**1a** could not take such a regular arrangement because of the bent structure. Moreover, the carbamate residues of *cis*-**1a** are unfavorably concealed behind the bent *cis*-azobenzene moieties so that the carbamate residues may not effectively be able to interact with racemates. This must result in a decrease in adsorbing ability and a lowering of the chiral recognition ability of *cis*-**1a**.

The different conformations of these isomers also affected their morphology and solubility; *trans*-**1a** and -**2a** formed a liquid-crystalline phase in a concentrated THF solution, but *cis*-**1a** and -**2a** did not form it under

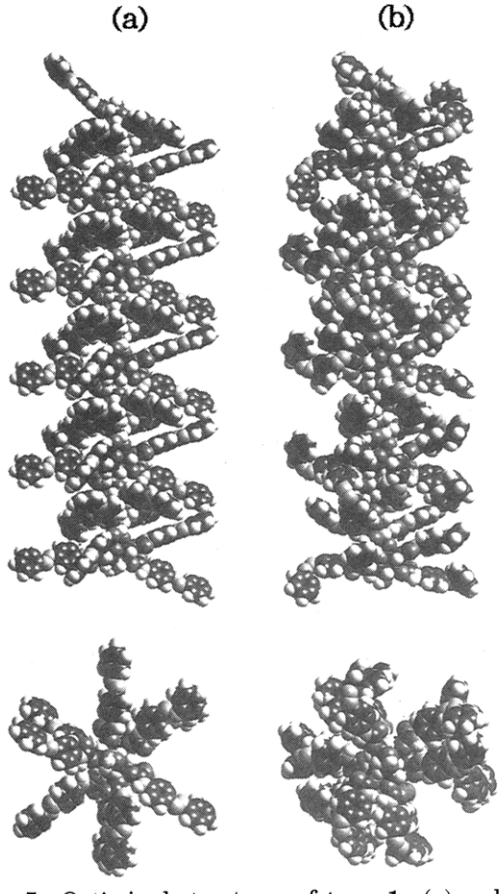


Figure 5. Optimized structures of *trans*-**1a** (a) and *cis*-**1a** (b): (top) along the chain axis (bottom) perpendicular to the chain axis.

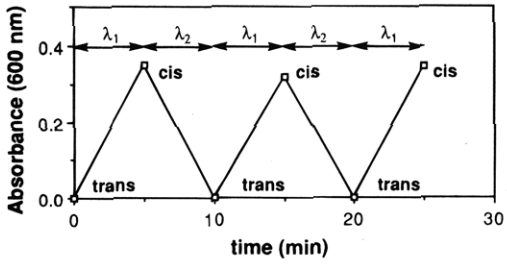


Figure 6. Photocontrol of solubility of **2a** in ethyl acetate (2 mg/mL) upon photoirradiation of λ_1 ($340 < \lambda_1 < 400$) and λ_2 (>470 nm). Irradiation time: 5 min.

the same conditions.[12] In addition, solubility of the polysaccharide derivative was controlled by the *trans–cis* photoisomerization of the pendant azobenzene moieties. The solubility change was followed by measuring the absorbance at 600 nm wavelength where the polysaccharide derivative has no absorption. Upon irradiation of light (340–400 nm) a clear solution of *trans*-**2a** in ethyl acetate in a 1.0 mm quartz cell became turbid during the *cis* isomerization and the solution became clear upon photoirradiation in the course of *trans* isomerization. Hence, the solubility of the polysaccharide derivative can be controlled reversibly by light as a switch (Figure 6).

The results of enantioselective adsorption on the membranes consisting of regioselectively carbamoylated cellulose and amylose (**1b**, **1c**, **2b**, and **2c**) are shown in Table 2. There existed no significant difference in the enantioselective adsorption ability between **1b** and **1c**, and **2b** and **2c**. The *trans* membranes also showed higher chiral recognition to the analytes than the *cis*

Table 2. Enantioselective Adsorption on 1b, 1c, 2b, and 2c Membranes[a]

		trans[b]		*cis*[c]		*cis*-to-*trans*[d]	
racemate	polym	% ee[e]	amt[f] (wt %)	% ee[e]	amt[f] (wt %)	% ee[e]	amt[f] (wt %)
5	**1b**	50.7 (−)	2.0	23.0 (−)	1.4	37.8 (−)	2.0
5	**1c**	48.0 (−)	2.0	30.3 (−)	1.4	47.7 (−)	2.2
6	**1b**	33.0 (+)	1.5	20.9 (+)	1.7	27.5 (+)	1.7
6	**1c**	28.3 (+)	1.3	22.5 (+)	1.6	29.4 (+)	1.9
3	**2b**	28.6 (+)	0.7	21.5 (−)	0.7	20.9 (−)	0.9
3	**2c**	32.1 (−)	0.9	31.7 (−)	0.8	28.0 (−)	0.9
4	**2b**	29.2 (−)	2.7	27.6 (−)	2.7	29.0 (−)	2.7
4	**2c**	31.8 (−)	2.8	26.5 (−)	2.6	30.2 (−)	2.3

[a] Average values of several independent runs. [b] The membrane was prepared by casting a THF solution of the *trans* isomer. [c] The membrane was prepared by casting a THF solution of the *cis* isomer (*cis* content; 65−75%). [d] The membrane prepared by casting a THF solution of the *cis* isomer was isomerized to the *trans* form. [e] The enantioselectivities were reproducible in about ±5% ee on repeated runs. In parentheses is shown the sign of optical rotation of the enantiomer preferentially adsorbed on the membranes. [f] The amount of analytes adsorbed on the polymer.

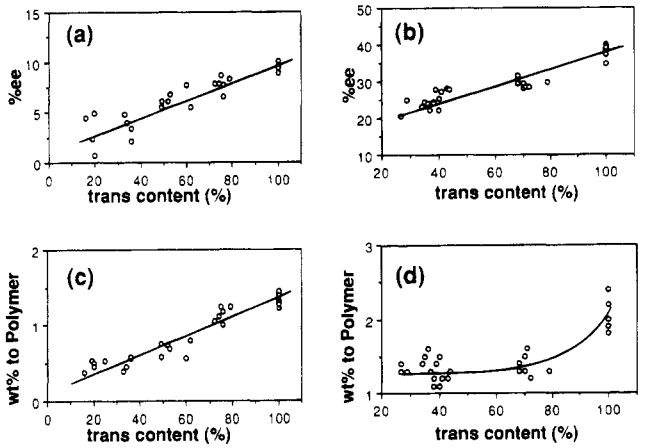


Figure 7. Effect of the *trans* content on the % ee and amount of analytes adsorbed on the membranes in the enantioselective adsorption of **4** on **1a** (a and c) and **5** on **1b** (b and d).

membranes, particularly to oxprenolol **5**, a β-adregenic drug (β-blocker). The (*S*)-(−) isomer of **5**, which is much more effective than the (*R*)-(+) isomer,[15,22] was preferentially adsorbed on the *trans* membranes of **1b** and **1c**. Oxprenolol rich in (*S*) isomer up to 50% ee was obtained by the single adsorption−desorption procedure. The change in % ee and amount of the analytes adsorbed on the membranes during the *cis*-to-*trans* isomerization is shown in Figure 7. The increase in the *trans* content tends to increase the % ee and amount of the analytes.

Photocontrol of Enantioselective Adsorption. Because the membranes used for the enantioselective adsorption experiments were too thick to quantitatively isomerize from the *trans* to *cis* form using light, the *cis* membrane coated with a small amount of **1c** (5 mg) and then used in the experiments for the photocontrol of chiral recognition. The *cis* membrane immediately after preparation from the *trans* isomer (*cis* content, *ca.* 80%) can adsorb the analyte **5** with 20% ee. After photoisomerizing it to the *trans* form, **5** of 43% ee was adsorbed on the membrane. This membrane was photoisomerized to the *cis* form (*cis* content, ca. 80%), which adsorbed the same analyte with 38% ee. This enantioselective adsorption could be repeated as shown in Figure 8 and the enantioselectivity was reversibly changed during the course of the photoisomerization. When the azo group of the membrane was *trans*, **5** of 43% ee was adsorbed, and when it was *cis*, **5** of 38% ee was adsorbed. Thus, the photocontrol of chiral recognition was for the first time realized using the photoresponsive chiral polymer membranes.

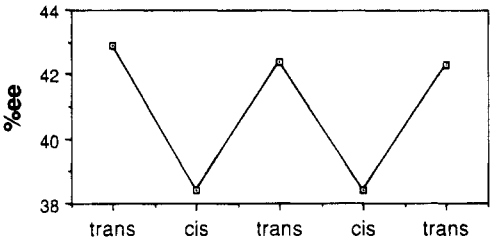


Figure 8. Change of % ee of **5** adsorbed on the **1c** membrane during the *trans*−*cis* isomerization (irradiation time = 4 h for the *trans*−*cis* isomerization, 2 h for the *cis*−*trans* isomerization). The *trans* and *cis* contents were 100 and 80%, respectively.

Experimental Section

Materials. Cellulose was obtained from Merck (Avicel). Amylose was a gift from Nakano Vinegar (degree of polymerization (DP) = 162 for **2a**, 190 for **2b** and **2c**). 3,5-Dimethylphenyl isocyanate was supplied from Daicel Chemical. 4-(Phenylazo)phenyl isocyanate was prepared by the method described previously.[12] Triphenylmethyl chloride was obtained from Tokyo Kasei. Pyridine was distilled over potassium hydroxide and stored under nitrogen. Racemic compounds, *trans*-2,3-diphenyloxirane (**3**) and 1-(9-anthryl)-2,2,2-trifluoroethanol (**6**), were purchased from Aldrich. Hydrochloric salt of oxprenolol (**5**) (Sigma) was neutralized before use. 1,2,2,2-Tetraphenylethanol (**4**) was prepared according to the reported method.[16] All other chemicals were obtained from commercial sources.

Cellulose Tris[[4-(phenylazo)phenyl]carbamate] (1a). This polymer was prepared by the reaction of excess 4-(phenylazo)phenyl isocyanate with cellulose in dry pyridine at 90 °C for 22 h and isolated as a methanol-insoluble fraction.[12] DP of Avicel was estimated to be *ca.* 200 from the GPC curve of cellulose tribenzoate.[12] GPC of **1a** showed very broad peaks, probably due to association in THF. $[\alpha]_D^{25}$ +94° (THF). IR (KBr): 3316 (ν_{NH}), 1731 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_{45}H_{37}N_9O_8$: C, 64.97; H, 4.48; N, 15.16. Found: C, 64.29; H, 4.77; N, 14.70.

Regioselectively carbamoylated cellulose (**1b** and **1c**) and amylose (**2b** and **2c**) were prepared in a manner similar to the reported procedures for the regioselective phenylcarbamoylation of the polysaccharides.[16] The detailed procedure for the preparation of **1b** is as follows.

1b. Cellulose (3.07 g, 18.9 mmol of glucose units) was allowed to react with triphenylmethyl chloride (21.1 g, 75.5 mmol), which can react with only the primary hydroxy group at the 6-position to form a trityl ether, in dry pyridine (150 mL) at 80 °C for 24 h. An excess of 3,5-dimethylphenyl isocyanate was then added to react with the hydroxy groups at the 2- and 3-positions and the remaining free hydroxy group at the 6-position. The obtained 2,3-bis[(3,5-dimethylphenyl)carbamoyl]-6-*O*-tritylcellulose was suspended in a large excess of methanol containing a small amount of hydrochloric acid so as to remove the trityl group at room temperature. The

cellulose 2,3-bis[(3,5-dimethylphenyl)carbamate] thus obtained (1.03 g) was allowed to react with a large amount of 4-(phenylazo)phenyl isocyanate (1.08 g, 4.85 mmol) in dry pyridine (30 mL) at 100 °C with stirring. After 14 h, the reaction mixture was poured into a large amount of methanol and the precipitated polymer **1b** was recovered by centrifugation and dried in vacuo at 60 °C; yield 0.69 g. The contents of (3,5-dimethylphenyl)carbamate and [4-(phenylazo)phenyl]carbamate residues were estimated by elemental analysis and ^{1}H NMR. $[\alpha]_D^{25}$ −21° (THF). IR (KBr): 3370 (ν_{NH}), 1738 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_{35}H_{37}N_4O_8$ ((3,5-dimethylphenyl)-carbamate:[4-(phenylazo)phenyl]carbamate = 2.5:0.5): C, 65.51; H, 5.81; N, 8.73. Found: C, 66.44; H, 5.52; N, 8.23.

1c. This polymer was prepared by an analogous method for **1b**. First, 6-*O*-tritylcellulose (1.51 g) was allowed to react with 3,5-dimethylphenyl isocyanate (0.53 g, 3.60 mmol) to carbamoylate the remaining hydroxy groups at the 6-position in dry pyridine at 90 °C for 6.5 h with stirring. To the reaction mixture was added 4-(phenylazo)phenyl isocyanate (0.59 g, 2.66 mmol). After 16 h, a large excess of 3,5-dimethylphenyl isocyanate (1.85 g, 12.6 mmol) was added and the reaction mixture was stirred at 90 °C for 24 h. The reaction mixture was then poured into a large amount of methanol, and the precipitated polymer was recovered by centrifugation and dried in vacuo at 60 °C. After the trityl groups were removed in a similar manner, the cellulose derivative (1.30 g) thus obtained was allowed to react with a large amount of 3,5-dimethylphenyl isocyanate (0.85 g, 5.64 mmol) to afford **1c** (0.69 g). $[\alpha]_D^{25}$ −18° (THF). IR (KBr): 3318 (ν_{NH}), 1740 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_{34.6}H_{37}N_{3.8}O_8$ ((3,5-dimethylphenyl)carbamate:[4-(phenylazo)phenyl]carbamate = 2.6:0.4): C, 65.53; H, 5.88; N, 8.40. Found: C, 65.28; H, 5.84; N, 8.22.

Similarly, amylose derivatives were prepared. Amylose tris-[[4-(phenylazo)phenyl]carbamate] (**2a**): $[\alpha]_D^{25}$ −529° (THF); IR (KBr) 3410, 3310 (ν_{NH}), 1738 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_{45}H_{37}N_9O_8$: C, 64.97; H, 4.48; N, 15.16. Found: C, 64.48; H, 4.78; N, 14.74. **2b**: $[\alpha]_D^{25}$ −63° (THF); IR (KBr) 3390 (ν_{NH}), 1738 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_{34.6}H_{37}N_{3.8}O_8$ ((3,5-dimethylphenyl)carbamate:[4-(phenylazo)phenyl]carbamate = 2.6:0.4): C, 65.53; H, 5.88; N, 8.40. Found: C, 66.10; H, 5.88; N, 8.26. (**2c**): $[\alpha]_D^{25}$ −146° (THF); IR (KBr) 3342 (ν_{NH}), 1744 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_{34.6}H_{37}N_{3.8}O_8$ ((3,5-dimethylphenyl)carbamate:[4-(phenylazo)phenyl]carbamate = 2.6:0.4): C, 65.53; H, 5.88; N, 8.40. Found: C, 66.46; H, 5.61; N, 8.24.

Measurements. The ^{1}H-NMR spectra were measured with a Varian XLS-500 (500 MHz) spectrometer using TMS as an internal standard. Optical rotation was measured with a JASCO DIP-181 Digital polarimeter using a quartz cell (0.5 dm) in THF (*c* 0.2−0.4 g dL^{-1}). The IR spectra were recorded on a JASCO IR 810 spectrophotometer as KBr pellets. The absorption and circular dichroism (CD) spectra of solutions were obtained with JASCO Ubest-55 and JASCO J-720L spectrophotometers, respectively, using a quartz cell with a path length of 1.0 or 0.1 mm. The absorption and CD spectra of films cast on a quartz plate were measured four times by rotating the sample quartz plate by 90, 180, and 270° from the first position around the axis of the incident light beam. The CD spectra were calibrated to the same molar concentration on the basis of the data of the absorption measurement. Chromatographic resolution was accomplished on a JASCO PU-980 chromatograph equipped with a UV detector (JASCO UV-970) by using a chiral column (250 × 4.6 (i.d.) mm) packed with cellulose tris[(3,5-dimethylphenyl)carbamate][13] or amylose tris[(3,5-dimethylphenyl)carbamate][14] as the CSPs.

Isomerization. Photoirradiation was carried out using a 400 W high-pressure mercury lamp and Toshiba filters. Azobenzene is well-known to isomerize from the *trans* to *cis* form under irradiation. The *cis* form returns thermally or photochemically to the *trans* form. As illustrated in Chart 1, the azobenzene pendant groups of the polysaccharide derivatives were isomerized from the *trans* to *cis* form with light (340−400 nm, UV-35 and UV-D36C filters). The *cis* isomer was photochemically (>470 nm, Y-47 filter) or thermally converted to the *trans* isomer. The isomerization in solutions was carried out in a quartz cell or a Pyrex sample bottle. The irradiation time for *trans*-to-*cis* and *cis*-to-*trans* isomerizations was *ca.* 40 and *ca.* 30 min, respectively, in the case of a THF solution of **1a** (0.2 mg/mL, 1 mm cell). Photoisomerization of the polysaccharide derivative membranes used in the enantioselective adsorption experiments was carried out in a hexane−2-propanol mixture (9/1 v/v). The irradiation time for the *trans*-to-*cis* and *cis*-to-*trans* isomerizations was *ca.* 4 and 2 h, respectively, in the case of the membrane prepared by casting a THF solution of **1c** (*ca.* 5 mg).

The *trans* percentage was calculated by the ratio of the absorbance maximum at around 350 nm to the absorption at an isosbestic point, assuming that the *trans* percentage was 100% immediately after the preparation of samples, and the absorbance of the *cis* isomer is negligible compared with that of the *trans* isomers.

Preparation of the Membrane. Since the membranes prepared by casting a THF solution of polysaccharide derivatives were brittle, a Teflon membrane filter (Advantec, 25 mm Ø, 0.10 μm pore) was used as a support. The *trans* and *cis* membranes were prepared by casting THF solutions of the *trans* and *cis* isomers (10 mg/mL), respectively, on the Teflon membrane filter followed by drying on a glass plate under nitrogen at room temperature under shielded light. The amount of the polymers coated on a Teflon membrane was about 10 mg. These membranes were quickly used for the enantiomer selective adsorption experiments. For the continuous enantioselective adsorption experiments, the membranes coated on a Teflon support with about 5 mg of the polysaccharide derivatives were used.

Enantioselective Adsorption. The enantioselective adsorption experiments using the *trans* membranes were carried out in the following way. First, the *trans* membrane was placed in a racemate solution (4 mg/4 mL in hexane−2 propanol (9/1)) at 15 °C for 60 min under shielded light. *trans*-2,3-Diphenyloxirane (**3**), 1,2,2,2-tetraphenylethanol (**4**), oxprenolol (**5**), and 1-(9-anthryl)-2,2,2-trifluoroethanol (**6**) were used as analytes. For the enantioselective adsorption with the membrane coated with *ca.* 5 mg of **1c**, the solution of racemic oxprenolol in a hexane−2-propanol (8/2) mixture was used. The membrane was taken out and washed with hexane−2-propanol (9/1) as quickly as possible to remove the racemic solution attached on the surface of the membrane. The membrane was then placed into 3 mL of hexane−2-propanol (7/3) at 30 °C for 30 min under shielded light to desorb the analyte adsorbed on the membrane. The amount and ee of the analyte adsorbed on the membrane were estimated by using the chiral HPLC columns.

The enantioselective adsorption experiments using the *cis* membranes were carefully carried out in a similar way under rigorously shielded light. After the enantioselective adsorption on the *cis* membrane was completed at 15 °C for 60 min, the *cis* membrane was taken out and washed with hexane−2-propanol. Part of the *cis* membrane was cut into a strip (*ca.* <0.2 mg), which was dissolved in a minimum amount of THF as quickly as possible to measure the absorption spectrum using a quartz cell with a path length of 0.1 mm. The *cis* percentage was estimated on the basis of the spectrum according to the method described previously. This process should be done before the desorption of the analyte at 30 °C, because the *cis* percentage may change during the desorption procedure. The *cis* percentage of the *cis* membranes thus estimated just after the enantioselective adsorption experiments was found to be about 65−80%. This clearly suggests that the thermal *cis*-to-*trans* isomerization of the *cis* membranes is rather slow within out experimental conditions.[17] Then, the *cis* membrane was placed into 3 mL of hexane−2-propanol (7/3) at 30 °C for 30 min under shielded light to desorb the analyte adsorbed on the membrane, and the amount and ee of the analyte adsorbed on the *cis* membrane were estimated by using the chiral HPLC columns. The *cis* membranes were stored in a refrigerator under shielded light and were used for further enantioselective adsorption experiments to investigate the effect of the *cis* contents in the enantioselective adsorption, as shown in Figure 7. The *trans* rich membranes (*trans* % = *ca.* 70) in Figure 7b,d were prepared by photochemical and thermal conversion of the *cis* membranes.

Molecular Modeling. Molecular modeling and molecular mechanics calculations were performed with the DREIDING force field[23] (version 2.01) as implemented in CERIUS[2] (Molecular Simulations Inc., MA) running on an Indigo[2]-Extreme graphics workstation (Silicon Graphics). The method used was similar to the previously reported one with a modification.[20] First, a full energy minimization of one unit of *trans*-**1a** was performed by a conjugate gradient method using the DREIDING force field until the root mean square value became less than 0.1 kcal/mol. Next, the optimized monomer was allowed to construct a trimer (*trans*-3mer) with a left-handed 3-fold (3/2) helix by Polymer Builder in CERIUS[2] according to the structure of cellulose tris(phenylcarbamate) reported by Zugenmaier et al.[18] The trimer was placed into a simulation cell ($x = 60, y = 60$, and $z = 15.35$ Å) using three-dimensional periodic boundary conditions by Crystal Builder in CERIUS[2]. The unit cell volume was expanded to the direction perpendicular to the polymer axis (z) to avoid interactions of the periodic polymer with neighboring ones in other cells. The energy minimization of the periodic structure was then performed. The resulting optimized trimer in the unit cell was connected to give a 15mer (*trans*-15mer). A *cis*-15mer was constructed on the basis of the *trans*-15mer by randomly changing azo groups from the *trans* to *cis* form. The obtained *cis*-15mer was further optimized by molecular mechanics calculations.

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Supporting Information Available: Figures of absorption and CD spectra of **1b**, **1c**, **2b**, and **2c** in THF, the **1a** film during the *trans*–*cis* photoisomerization, and absorption spectral changes of *cis* films of **1a**, **1b**, and **1c** during the *cis*–*trans* thermal isomerization or photoisomerization (5 pages). Ordering information is given on any current masthead page.

References and Notes

(1) Reviews: (a) Irie, M. *Adv. Polym. Sci.* **1990**, *94*, 27. (b) Ciardelli, F.; Pieroni, O.; Fissi, A.; Carlini, C.; Altomare, A. *Br. Polym. J.* **1989**, *21*, 97.
(2) (a) Irie, M.; Hayashi, K. *J. Macromol. Sci., Chem.* **1979**, *13*, 511. (b) Irie, M.; Hosoda, M. *Makromol. Chem., Rapid Commun.* **1985**, *6*, 533. (c) Irie, M.; Hirano, Y.; Hashimoto, S.; Hayashi, K. *Macromolecules* **1981**, *14*, 262.
(3) Irie, M.; Kungwatchakun, D. *Makromol. Chem., Rapid Commun.* **1985**, *5*, 879.
(4) Aoyama, M.; Watanabe, J.; Inoue, S. *J. Am. Chem. Soc.* **1990**, *112*, 5542.
(5) Yamamoto, H.; Nishida, A. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1477.
(6) (a) Ueno, A.; Takahashi, K.; Anzai, J.; Osa, T. *J. Am. Chem. Soc.* **1981**, *103*, 6410. (b) Kinoshita, T.; Sato, M.; Takizawa, A.; Tsujita, Y. *J. Am. Chem. Soc.* **1986**, *108*, 6399. (c) Sisido, M.; Ishikawa, Y.; Itoh, K.; Tazuke, S. *Macromolecules* **1991**, *24*, 3993. (d) Sisido, M.; Ishikawa, Y.; Harada, M.; Itoh, K. *Macromolecules* **1991**, *24*, 3999.
(7) Hohsaka, T.; Kawashima, K.; Sisido, M. *J. Am. Chem. Soc.* **1994**, *116*, 413.
(8) (a) Strzegowski, L. A.; Martinez, M. B.; Gowda, D. C.; Urry, D. W.; Tirrell, D. A. *J. Am. Chem. Soc.* **1994**, *116*, 813. (b) Murata, K.; Aoki, M.; Suzuki, T.; Harada, T.; Kawabara, H.; Komori, T.; Ohseto, F.; Ueda, O.; Shinkai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6664.
(9) (a) Ueno, A.; Yoshimura, H.; Saka, R.; Osa, T. *J. Am. Chem. Soc.* **1979**, *101*, 2779. (b) Ueno, A.; Tomita, Y.; Osa, Y. *Tetrahedron Lett.* **1983**, *24*, 5245. (c) Hamada, F. *Makromol. Chem., Rapid Commun.* **1993**, *14*, 279. (d) Hamada, F. *Makromol. Chem., Rapid Commun.* **1993**, *14*, 287.
(10) Shinkai, S.; Nakaji, T.; Ogata, T.; Shigematsu, K.; Manabe, O. *J. Am. Chem. Soc.* **1981**, *103*, 111.
(11) Ueno, A.; Saka, R.; Takahashi, K.; Osa, T. *Heterocycles* **1981**, *15*, 671.
(12) Okamoto, Y.; Sakamoto, H.; Hatada, K.; Irie, M. *Chem. Lett.* **1986**, 983.
(13) (a) Okamoto, Y.; Kawashima, M.; Hatada, K. *J. Am. Chem. Soc.* **1984**, *106*, 5357. (b) Okamoto, Y.; Kawashima, M.; Hatada, K. *J. Chromatogr.* **1986**, *363*, 173. (c) Okamoto, Y.; Aburatani, R.; Fukumoto, T.; Hatada, K. *Chem. Lett.* **1987**, 1857. (d) Okamoto, Y.; Aburatani, R.; Hatano, K.; Hatada, K. *J. Liq. Chromatogr.* **1988**, *11*, 2147. (e) Aburatani, R.; Okamoto, Y.; Hatada, K. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3606. (f) Kaida, Y.; Okamoto, Y. *Chirality* **1992**, *4*, 122.
(14) (a) Okamoto, Y.; Kaida, Y.; Aburatani, R.; Hatada, K. In *Chiral Separations by Liquid Chromatography*; Ahuja, S., Ed.; ACS Symposium Series 471; American Chemical Society: Washington, DC, 1991; pp 101–113. (b) Okamoto, Y.; Kaida, Y. *J. Chromatogr. A* **1994**, *666*, 403.
(15) (a) Yashima, E.; Noguchi, J.; Okamoto, Y. *Chem. Lett.* **1992**, 1959. (b) Yashima, E.; Noguchi, J.; Okamoto, Y. *J. Appl. Polym. Sci.* **1994**, *54*, 1087.
(16) (a) Kaida, Y.; Okamoto, Y. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2225. (b) Yashima, E.; Fukaya, H.; Okamoto, Y. *J. Chromatogr. A* **1994**, *677*, 11.
(17) The *cis* form of azobenzene residues in the *cis* films thermally decays gradually to the *trans* form with time. However, the thermal isomerization rate of the *cis* films is slow enough, and we could get reliable data on the enantioselective adsorption using the *cis* films. The decay of the *cis* to *trans* form of all the *cis* membranes (**1a**–**2c**) prepared by casting THF solutions of the *cis* isomers on a quartz cell was followed by absorption measurements. The *cis* percentage of *cis*-**1a** film changed from 80 to 73% after standing for 1 h at ambient temperature (*ca.* 25 °C) under shielded light, and to 62 and 32% after 6 and 43 h, respectively. Cis %: *cis*-**1b** 93 (0 h), 90 (1 h), 80 (6 h), 62 (24 h); *cis*-**1c** 89 (0 h), 87 (1 h), 70 (6 h), 52 (24 h); *cis*-**2a** 88 (0 h), 75 (3 h), 65 (6 h), 48 (24 h); *cis*-**2b** 88 (0 h), 82 (1 h), 68 (6 h), 47 (24 h); *cis*-**2c** 89 (0 h), 80 (3 h), 73 (6 h), 50 (24 h). The absorption spectral changes of the *cis* films (**1a**, **1b**, and **1c**) are available in the supporting information.
(18) Vogt, U.; Zugenmaier, P. *Ber. Bunsen-Ges. Phys. Chem.* **1985**, *89*, 1217.
(19) Vogt, U.; Zugenmaier, P. Report at the European Science Foundation Workshop on Specific Interactions in Polysaccharide Systems, Uppsala, 1983.
(20) Yashima, E.; Yamada, M.; Okamoto, Y. *Chem. Lett.* **1994**, 579.
(21) Yashima, E.; Yamada, M.; Okamoto, Y. *J. Chromatogr. A* **1995**, *694*, 347.
(22) Hamaguchi, S.; Hasegawa, J.; Kawahara, H.; Watanabe, K. *Agric. Biol. Chem.* **1984**, *48*, 2055.
(23) (a) Mayo, S. L.; Olafson, B. D.; Goddard, W. A., III *J. Phys. Chem.* **1990**, *94*, 8897. (b) Rappe, A. K.; Goddard, W. A., III *J. Phys. Chem.* **1991**, *95*, 3358.

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