Synthesis, Chiroptical Properties, and Chiral Recognition Ability of Optically Active Polymethacrylamides Having Various Tacticities

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ABSTRACT: The radical polymerization of optically active methacrylamides, such as *N*-[(*R*)-(+)- α -methylbenzyl]methacrylamide, *N*-[(*R*)-(–)-1-cyclohexylethyl]methacrylamide, *N*-[(*R*)-(+)-1-(1-naphthyl)ethyl]methacrylamide, and *N*-[(1*R*,2*S*)-(–)-1-(2-indanol)]methacrylamide, was carried out under various conditions. The polymerization in the presence of ytterbium trifluoromethanesulfonate [Yb(OTf)₃] produced isotactic-rich polymers compared with those obtained without the Lewis acid. The specific rotations and the circular dichroism spectral patterns of the obtained polymers varied with the tacticities, suggesting that the tacticities influence the secondary structures of the polymers. The IR spectra of the polymers indicated that the isotactic polymers favorably formed intramolecular hydrogen bonds. The chiral recognition ability of the optically active polymers immobilized on silica gel was evaluated as the chiral stationary phases for high-performance liquid chromatography (HPLC). [DOI 10.1295/polymj.37.299]

KEY WORDS Radical Polymerization / Lewis Acid / Tacticity / Optically Active Polymer / Chiral Recognition / HPLC / Chiral Stationary Phase /

Recently, we found that Lewis acids, such as rare earth metal trifluoromethanesulfonates (triflates), catalytically change the stereoregularity of polymers during the radical polymerization of acrylamides^{1–3} and methacrylamides.^{1,4,5} The conventional radical polymerizations of methacrylates⁶ and methacrylamides,^{4,5,7} except for those having bulky side chains,^{8,9} generally produce a syndiotactic-rich polymer due to the steric repulsion between the side chains. On the other hand, Lewis acids interact with the monomers and the propagating chain-end to change the stereochemistry of the polymerization to isotactic-selective manner.¹ In our previous study,⁵ the polymerization of *N*-[(*R*)- α -methoxycarbonylbenzyl]methacrylamide ((*R*)-**1**) in the presence of Yb(OTf)₃ produced an isotactic-rich polymer, whereas a syndiotactic polymer was obtained during the conventional radical polymerization without the Lewis acid. The tacticity of polymers often influences their physical properties and functions. For instance, poly[(meth)acrylamide]s have different solubilities,^{1,2,10} thermo-responsibilities,⁴ hydrogen bonding formations, and conformations depending on the tacticity.¹¹ We also demonstrated that the chiral recognition ability of poly[(*R*)-**1**] was affected by the stereoregularity.⁵ In this study, the radical polymerizations of four methacrylamides bearing optically

active groups, *N*-[(*R*)-(+)- α -methylbenzyl]methacrylamide ((*R*)-**2**), *N*-[(*R*)-(–)-1-cyclohexylethyl]methacrylamide ((*R*)-**3**), *N*-[(*R*)-(+)-1-(1-naphthyl)ethyl]methacrylamide ((*R*)-**4**), and *N*-[(1*R*,2*S*)-(–)-1-2-indanol]methacrylamide ((–)-**5**), in the presence and absence of Lewis acids were carried out to synthesize the polymethacrylamides having different tacticities, and the relationship between the stereoregularity and the chiroptical properties of the polymers was discussed.

Poly[(meth)acrylamide]s bearing the optically active side chain are known to show a high chiral recognition ability for many polar racemates, and have been used as the chiral stationary phase (CSP) for high-performance liquid chromatography (HPLC) with the aim of resolving racemic pharmaceuticals.^{12,13} Blaschke *et al.* reported that the optically active poly(**3**) can completely separate the enantiomers of thalidomide, whose (*S*)-isomer causes a teratogenic effect.¹³ The stereoregularities of the poly[(meth)acrylamide]s prepared by conventional radical polymerization are not sufficiently controlled. However, a controlled stereoregular structure may result in a superior chiral separation ability due to the regular arrangement of the chiral sites. A helical structure is one of the most interesting conformations that stereoregular polymers can form.¹⁴ Many polymer-based

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Structure 1

CSPs, including polysaccharides¹⁵ and poly(trityl methacrylate)s synthesized by asymmetric polymerization,^{14,16} show a high chiral recognition ability based on their regular structures, such as a one-handed helical conformation. Nakahira *et al.*¹¹ suggested that the optically active polymethacrylamides derived from isotactic poly(methacrylic acid) may form a helical structure in solution, but the chiral recognition ability of the isotactic polymethacrylamide was not evaluated. Interestingly, Blaschke *et al.* reported¹² that the optically active polymethacrylamides directly synthesized *via* the radical polymerization of the corresponding chiral monomers had a higher chiral recognition ability compared with the optically active polymethacrylamides derived from poly(methacryloyl chloride). In the present study, the optically active polymethacrylamides were immobilized by radical copolymerization onto a silica gel having a methacrylate residue on the surface, and their chiral recognition abilities as a CPS were evaluated.

EXPERIMENTAL

Materials

Methacryloyl chloride was distilled before use. Triethylamine was dried over KOH and distilled. Dehydrated solvents, including dichloromethane, chloroform, 1,4-dioxane, tetrahydrofuran (THF), methanol, and benzene, were purchased from Kanto Chemical, and used as received. 2,2'-Azobisisobutyronitrile (AIBN) was recrystallized from methanol. Lewis acids, such as ytterbium triflate (Yb(OTf)₃), yttrium triflate (Y(OTf)₃), and scandium triflate (Sc(OTf)₃) (Aldrich), were dried under vacuum before use. (*R*)- α -Methylbenzylamine, (*R*)-1-cyclohexylethylamine, (*R*)-1-(1-naphthyl)ethylamine, and (1*R*,2*S*)-*cis*-1-amino-2-indanol (Aldrich) were used as commercially obtained. Macroporous silica gel (Daiso gel SP-1000, pore size 100 nm, particle size 7 μ m) and 2-methacryloyloxyethyl isocyanate were kindly supplied by Daiso Chemical and Showa Denko, respectively. All Other reagents were purified as reported in previous papers.^{1,2,4,5}

Monomer Synthesis

The monomers were synthesized from methacryloyl chloride and the corresponding amines as previously reported.⁵

N-[(*R*)-(+)- α -Methylbenzyl]methacrylamide ((*R*)-2). Yield 48%. Mp 92.7–93.1 °C. (Mp 91–92 °C¹⁷) [α]_D²⁵ +48.9°. [α]₃₆₅²⁵ +212.8°.

N-[(*R*)-(-)-1-Cyclohexylethyl]methacrylamide ((*R*)-3). Yield 65%. Mp 93.2–93.7 °C. (Mp 92 °C¹⁷) [α]_D²⁵ -17.5°. [α]₃₆₅²⁵ -43.8°.

N-[(*R*)-(+)-1-(1-Naphthyl)ethyl]methacrylamide ((*R*)-4). Yield 71%. Mp 112.9–113.5 °C. (Mp 112 °C¹⁷) [α]_D²⁵ +2.6°. [α]₃₆₅²⁵ +27.7°.

N-[(1*R*,2*S*)-(-)-1-(2-Indanol)]methacrylamide ((-)-5). Yield 54%. ¹H NMR (400 MHz, CDCl₃, δ): 2.0 (s, 3H, CH₃), 2.27 (d, 1H, *J* = 4.8 Hz, OH), 2.9–3.2 (m, 2H, CH₂), 4.66 (m, 1H, CH₂OH), 5.39 (s, 1H, vinyl), 5.40–5.43 (m, 1H, CHN), 5.80 (s, 1H, vinyl), 6.49 (s, 1H, NH), 7.2–7.3 (m, 4H, aromatic). IR (KBr) 3465, 3309, 2950, 1651, 1613, 1542, 1399, 1175, 1056, 926, 748 cm⁻¹. Mp 98.4–99.0 °C. [α]_D²⁵ -33.4°. [α]₃₆₅²⁵ -154.8°.

Polymerization Procedure

Polymerization was carried out in a glass ampule under a nitrogen atmosphere. A Lewis acid, AIBN, and a monomer were placed in the ampule and dried under vacuum for 1 h. The polymerization solvent was then added to the ampule to obtain a solution. The polymerization at 60 °C was initiated by heating the ampule in an oil bath. The polymerizations at lower temperatures were carried out under UV irradiation using a 500 W high-pressure mercury lamp. After the polymerization, the polymers were precipitated in a large excess of a solvent. The polymers were separated by centrifugation, and dried *in vacuo* at 60 °C.

Introduction of Methacryloyl Groups on Silica Gel (6)¹⁸

The procedure is shown in Scheme 1. Macroporous silica gel (50 g) was placed in a 1 L flask equipped with a three-way cock, and dried at 180 °C for 2 h in an oil bath. Dehydrated benzene (500 mL), 3-aminopropyl-ethoxysilane (20 mL), and pyridine (3 mL) were added

Scheme 1. Introduction of a vinyl group on silica surface.

to the flash, and the mixture was refluxed for 12 h at 90 °C. The silica gel was filtered, successively washed with methanol, acetone, and hexane, and dried at 60 °C *in vacuo*. The resulting silica gel (4.2 g) was placed in a flask and treated with 2-methacryloyloxyethyl isocyanate (0.23 g) in toluene (12 mL) at 90 °C for 5 h. The mixture was filtered, washed with THF, methanol, acetone, and hexane, and dried at room temperature *in vacuo* to obtain the silica gel **6**. The content of the organic parts on the silica gel **6** was determined to be 4.2% by thermogravimetry (TG).

Measurements

The ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 spectrometer (400 MHz for ^1H). The number-average molecular weight (M_n) and the polydispersity (M_w/M_n) of the polymers were determined by size exclusion chromatography (SEC) calibrated with standard polystyrenes using a JASCO RI-930 detector and a set of TSK-gel α -3000 and α -M columns connected in series with a 0.1 mol/L LiCl solution in *N,N*-dimethylformamide (DMF) as the eluent at 40 °C. The SEC was measured on a Shodex GPC-system-21 equipped with a Shodex RI-71S detector and a set of Shodex KF806L, KF803, and KF800R columns connected in series. The infrared (IR) spectra were recorded using a JASCO FT/IR-620 spectrometer. The melting point was measured in a glass capillary tube using a Buchi apparatus at a heating rate of 1 °C/min. The thermogravimetry (TG) analysis was carried out using a Seiko EXSTRA 6000 system. The optical rotation was measured in THF at room temperature using a JASCO P-1030 polarimeter. The circular dichroism (CD) spectra were measured using a JASCO J-720L spectrometer. The chromatographic resolution was performed using a JASCO PU-1580 equipped with JASCO MD-910 (UV) and CD-1595YS detectors at room temperature. The dead time (t_0) was estimated using 1,3,5-tri(*tert*-butyl)benzene.

RESULTS AND DISCUSSION

Lewis Acid-catalyzed Polymerization of Optically Active Methacrylamides and the Chiroptical Properties of the Obtained Polymers

The results of the polymerization of (*R*)-**2** in the absence or presence of Lewis acids under various conditions are shown in Table I. The tacticities of the poly-[(*R*)-**2**]s were determined by ^{13}C NMR spectroscopy on the basis of the peak splitting of carbonyl (175–178 ppm), α -methyl (16–24 ppm), methyl carbons on the side chain (around 21 ppm), and quaternary carbon of the main chain (44–55 ppm) according to the reported assignments for polymethacrylamides having an analogous structure.^{4,7} The spectra of various poly-[(*R*)-**2**]s are shown in Figure 1. The polymerization in the absence of Lewis acids at 60 °C resulted in syndiotactic-rich polymers with *rr* = 53–66%. The polymerization temperature slightly influenced the tacticity, and a more syndiotactic polymer (*rr* = 69%) was obtained in THF at lower temperatures, similar to the polymerizations of methacrylates¹⁸ and other methacrylamides.^{4,5} However, a significant decrease in the polymer yield was observed at lower temperatures. On the other hand, Lewis acids, such as $\text{Sc}(\text{OTf})_3$, $\text{Yb}(\text{OTf})_3$, and $\text{Y}(\text{OTf})_3$, increased the isotactic-selectivity during the polymerizations of (*R*)-**2**. In THF, $\text{Yb}(\text{OTf})_3$ and $\text{Y}(\text{OTf})_3$ were more effective than $\text{Sc}(\text{OTf})_3$. The effects of the Lewis acids strongly depended on the solvent, and the isotacticity of the polymers at 60 °C decreased in the order of methanol > THF > 1,4-dioxane > chloroform. The polymerization at lower temperatures in the presence of $\text{Yb}(\text{OTf})_3$ in methanol afforded a polymer having a higher isotacticity, in relatively high yields, although the polymerization without the Lewis acids resulted in a very low yield. The polymer with the highest isotacticity (*mm* = 70%) was obtained during the polymerization at 0 °C in the presence of an equimolar amount of $\text{Yb}(\text{OTf})_3$ to the monomer (1 mol/L). The polydisper-

Table I. Radical polymerization of (*R*)-**2** in the absence and presence of Lewis acids under various conditions^a

Entry	Lewis acid (mol/L)	Solvent	Temp. (°C)	Yield ^b (%)	M_n^c ($\times 10^{-4}$)	M_w/M_n^c	Tacticity ^d (mm/mr/rr)	$[\alpha]_{365}^e$ (deg)
1	none	THF	60	60	1.38	1.88	0/41/59	+241.7
2	Yb(OTf) ₃ (0.1)	THF	60	88	2.49	3.38	32/53/15	+116.4
3	Yb(OTf) ₃ (0.1)	THF	60	92	2.27	3.06	33/55/15	+150.3
4	Sc(OTf) ₃ (0.1)	THF	60	83	1.37	2.10	25/53/22	+181.7
5	none	1,4-dioxane	60	60	2.11	2.45	0/43/57	+210.1
6	Yb(OTf) ₃ (0.1)	1,4-dioxane	60	96	2.94	4.46	24/57/19	+161.9
7	none	chloroform	60	70	1.38	2.09	0/47/53	+234.4
8	Yb(OTf) ₃ (0.1)	chloroform	60	96	2.39	2.74	21/59/20	+173.8
9	none	methanol	60	56	2.07	1.63	0/34/66	+219.0
10	Yb(OTf) ₃ (0.1)	methanol	60	90	2.85	3.20	40/46/14	+51.6
11	none	THF	20	28	1.48	1.56	0/31/69	+216.5
12	Yb(OTf) ₃ (0.2)	THF	20	56	2.60	1.68	33/50/17	+64.8
13	none	methanol	20	10	3.17	1.87	—	—
14	Yb(OTf) ₃ (0.2)	methanol	20	59	2.40	2.98	57/34/9	−55.3
15	none	methanol	0	4	3.39	1.79	—	—
16	Yb(OTf) ₃ (0.2)	methanol	0	35	2.33	2.59	58/33/9	−146.3
17	Yb(OTf) ₃ (0.5)	methanol	0	47	— ^f	— ^f	66/26/8	−292.4
18	Yb(OTf) ₃ (1.0)	methanol	0	53	— ^f	— ^f	70/25/5	— ^g

^a[(*R*)-**2**]₀ = 1.0 mol/L, [AIBN]₀ = 0.02 mol/L (with UV irradiation (entries 11–18)), time = 24 hr. ^bDiethyl ether- and water-insoluble part. ^cDetermined by SEC in DMF (0.1 mol/L LiCl) at 40 °C (polystyrene standard). ^dDetermined by ¹³C NMR in DMSO-*d*₆ at 80 °C. ^eIn THF. ^fInsoluble in DMF. ^gInsoluble in THF.

Figure 1. ¹³C NMR spectra of poly[(*R*)-**2**]s prepared under various conditions. X denoted impurities [DMSO-*d*₆, 80 °C, 100 MHz].

sities (M_w/M_n) of the polymers prepared in the presence of the Lewis acids were broader than those obtained without the Lewis acids.

The tacticity of the poly[(*R*)-**2**]s influenced the chiroptical properties, such as the optical rotations and circular dichroism (CD). The plots of the specific ro-

Figure 2. Specific rotations of poly[(*R*)-2]s (10 mg/mL) having various tacticities in THF at room temperature.

Figure 3. CD spectra of (*R*)-2 (a) and poly[(*R*)-2]s having various tacticities (b–e) [THF, rt].

tations at 354 nm versus the isotacticity are shown in Figure 2. The syndiotactic polymers prepared in the absence of the Lewis acids showed similar specific rotation values ($[\alpha]_{365}^{25} = +210$ – 242°) to that of the (*R*)-2 monomer ($+213^\circ$). The absolute value of the specific rotation decreased with an increase in the isotacticity below $m = 63\%$ (40% of mm) and above 74% (57% of mm), negative $[\alpha]_{365}$ values were observed. The specific rotations increased in the negative direction with an increase in the isotacticity. The specific rotation of poly[(*R*)-2] with mm = 66% reached $[\alpha]_{365}^{25} = -292^\circ$, although that of poly[(*R*)-2] having mm = 70% could not be determined due to its insolubility.

Figure 3 shows the CD spectra of poly[(*R*)-2]s obtained in the absence and presence of a Lewis acid. The positive absorption at 217 nm and the negative one at 228 nm were enhanced with an increase in the

Figure 4. IR spectra of the NH region of poly[(*R*)-3]s having various tacticities.

isotacticity. These results indicate that the tacticity affects the conformation of the poly[(*R*)-2]s. A one-handed-helical structure may be partly induced on the main chain depending on the stereoregular structure.

In the IR spectra of poly[(*R*)-2]s, two peaks around 3445 and 3315 cm^{-1} due to the free NH and the hydrogen-bonded one, respectively, were observed (Figure 4). The relative peak intensity of the hydrogen-bonded NH increased with an increase in the isotacticity. The NH groups in the isotactic sequences appear to efficiently form intramolecular hydrogen-bonds. Therefore, the polymer structure in solution may be varied depending on the polarity of solvents. Polar solvents may cleavage the intramolecular hydrogen-bond to induce a conformational change of the polymer chain.

The results of the polymerization of (*R*)-3, (*R*)-4, and (–)-5 are summarized in Table II. Although the detailed tacticities of the obtained polymers could not be determined, the stereoregularity of the obtained polymers can be roughly estimated from the absorption patterns of the carbonyl peaks in the ^{13}C NMR measurement. Figure 5 shows the carbonyl region of the ^{13}C NMR spectra of the poly[(*R*)-3]s. The polymers prepared in the presence of $\text{Yb}(\text{OTf})_3$ showed peaks at lower magnetic fields compared with those obtained without the Lewis acids. From the polymer-

Table II. Radical polymerization of (*R*)-**3**, (*R*)-**4**, and (–)-**5** in the absence and presence of Lewis acids under various conditions^a

Entry	Monomer	Lewis acid (mol/L)	Solvent	Temp. (°C)	Yield ^b (%)	M_n^c ($\times 10^{-4}$)	M_w/M_n^c	$[\alpha]_{365}^e$ (deg)
19	(<i>R</i>)- 3	none	THF	60	55	1.59	1.33	–71.6
20	(<i>R</i>)- 3	Y(OTf) ₃ (0.1)	THF	60	83	2.29	1.53	–100.4
21	(<i>R</i>)- 3	Yb(OTf) ₃ (0.1)	THF	60	86	2.02	1.44	–100.2
22	(<i>R</i>)- 3	Sc(OTf) ₃ (0.1)	THF	60	58	1.63	1.30	–93.9
23	(<i>R</i>)- 3	none	chloroform	60	38	1.82	1.55	–66.0
24	(<i>R</i>)- 3	Yb(OTf) ₃ (0.1)	chloroform	60	73	1.69	1.41	–79.2
25	(<i>R</i>)- 3	none	methanol	60	44	1.65	1.29	–53.1
26	(<i>R</i>)- 3	Yb(OTf) ₃ (0.1)	methanol	60	88	1.64	1.37	–109.4
27	(<i>R</i>)- 3	none	methanol	20	17	1.48	1.30	—
28	(<i>R</i>)- 3	Yb(OTf) ₃ (0.1)	methanol	20	23	1.35	1.51	–117.4
29	(<i>R</i>)- 3	Yb(OTf) ₃ (0.2)	methanol	20	27	— ^f	— ^f	— ^g
30	(<i>R</i>)- 3	Yb(OTf) ₃ (0.5)	methanol	20	43	— ^f	— ^f	— ^g
31	(<i>R</i>)- 3	Yb(OTf) ₃ (1.0)	methanol	20	56	— ^f	— ^f	— ^g
32	(<i>R</i>)- 4	none	THF	60	87	2.23	1.95	–38.1
33	(<i>R</i>)- 4	Yb(OTf) ₃ (0.1)	THF	60	98	4.50	3.53	–271.5
34	(<i>R</i>)- 4	none	THF	0	14	1.25	2.58	—
35	(<i>R</i>)- 4	Yb(OTf) ₃ (0.1)	THF	0	20	1.24	2.36	–324.1
36	(<i>R</i>)- 4	Yb(OTf) ₃ (0.5)	THF	0	17	1.20	4.23	–324.0
37	(–)- 5	none	methanol	60	88	5.27	2.72	+157.6
38	(–)- 5	Yb(OTf) ₃ (0.1)	methanol	60	90	3.44	2.91	+80.9
39	(–)- 5	none	chloroform	60	79	11.2	3.00	+152.4
40	(–)- 5	Yb(OTf) ₃ (0.1)	chloroform	60	99	9.62	2.92	+86.9
41	(–)- 5	none	chloroform	0	83	4.75	2.89	+147.0
42	(–)- 5	Yb(OTf) ₃ (0.1)	chloroform	0	70	6.59	2.66	+81.6

^a[Monomer]₀ = 1.0 mol/L, [AIBN]₀ = 0.02 mol/L (with UV irradiation (entries 27–31, 34–36, 41–42)), time = 24 hr. ^bMethanol-insoluble part (entries 19–31, 37–42), diethyl ether- and water-insoluble part (entry 32–36). ^cDetermined by SEC in DMF (0.1 mol/L LiCl) at 40 °C (polystyrene standard). ^dDetermined by ¹³C NMR in DMSO-*d*₆ at 80 °C. ^eIn THF. ^fInsoluble in DMF. ^gInsoluble in THF.

ization of poly[(*R*)-**2**]s and other polymethacrylamides, the isotactic-rich polymers were obtained in the presence of Yb(OTf)₃ and the syndiotactic polymers without Lewis acids. During the polymerization of (*R*)-**3**, the effect of Yb(OTf)₃ and Y(OTf)₃ were more significant than that of Sc(OTf)₃, and methanol was the most effective solvent, similar to the polymerization of (*R*)-**2**. However, for (–)-**5**, chloroform was a better solvent for obtaining the isotactic polymer than methanol.

The specific rotations of poly[(*R*)-**3**]s increased with an increase in the isotacticity. Although the $[\alpha]_{365}$ value of the syndiotactic poly[(*R*)-**3**] prepared in the absence of Lewis acids in methanol at 60 °C was –53°, the polymer prepared in methanol at 20 °C in the presence of 10 mol % Yb(OTf)₃ to the monomer showed –117°. The specific rotation ($[\alpha]_{365}$ = –324°) of the isotactic poly[(*R*)-**4**] prepared in the presence of 10 mol % Yb(OTf)₃ in THF at 0 °C was significantly different from that (–38°) of the syndiotactic polymer. The specific rotation of the poly[(–)-**5**]s also changed from +158° to +81° depending on the tacticity.

The CD spectra of the (*R*)-**3** monomer and poly-

[(*R*)-**3**]s prepared in the absence and presence of Yb(OTf)₃ are shown in Figure 6. Compared with the polymer obtained without the Lewis acid, the polymer prepared in the presence of Yb(OTf)₃ showed more intense peaks around 224 nm and below 210 nm. These results indicate that the stereoregularity of the poly[(*R*)-**3**]s, poly[(*R*)-**4**]s, and poly[(–)-**5**]s also strongly influence the chiroptical properties, similar to those observed for the poly[(*R*)-**2**]s.

Immobilization of Optically Active Polymethacrylamides on Silica Gel

The optically active polymethacrylamides were immobilized on silica gels by the radical copolymerization of silica gel **6** having methacrylate residues on the surface with the methacrylamides [(*R*)-**2**, (*R*)-**3**, (*R*)-**4**, and (–)-**5**] in the absence or presence of Yb(OTf)₃. The immobilization conditions and the amount of polymethacrylamides immobilized on **6** are summarized in Table III. The TG analysis of the obtained polymer-immobilized silica gels indicated that 5–15 wt % of the polymers were fixed on the silica gel. Although the tacticities of the polymers immobilized on the silica gel could not be directly determined, chiral

Structure 2

Figure 5. ^{13}C NMR spectra of the carbonyl region of poly-[(*R*)-3]s prepared under various conditions [DMSO- d_6 , 80 °C, 100 MHz].

packing materials prepared in the absence and presence of $\text{Yb}(\text{OTf})_3$ must contain syndiotactic- and isotactic-rich polymers, respectively.

Figure 6. CD spectra of (*R*)-3 (a) and poly[(*R*)-3]s prepared in the absence (b) or presence of $\text{Y}(\text{OTf})_3$ (c) at 60 °C in methanol [THF, rt].

Enantioseparation on Optically Active Polymethacrylamides Immobilized on Silica Gel

The chiral recognition abilities of the optically active polymethacrylamides were evaluated by HPLC using a CSP immobilized on silica gel. The results of the resolution of eight racemates, including benzoic acid (7), 1,2,2,2-tetraphenylethanol (8), 1-(9-anthryl)-2,2,2-trifluoroethanol (9), *trans*-cyclopropanedicarboxylic acid dianilide (10), 2,2'-dihydroxy-6,6'-dimethylbiphenyl (11), 1,1'-bi-2-naphthol (12), 2,2'-dimethoxy-1,1'-binaphthyl (13), and 2,2'-dihydroxy-3,3'-dimethyl-1,1'-binaphthyl (14), are summarized in Tables IV and V. Here, capacity factors (k_1' and k_2') can be calculated as $(t_1 - t_0)/t_0$ and $(t_2 - t_0)/t_0$, where

Table III. Immobilization of polymethacrylamides on **6**^a

	Monomer	Yb(OTf) ₃	Solvent	Immobilized polymer ^c (wt % to silica gel)
SG-sP2	(<i>R</i>)- 2	absence	methanol	5.2
SG-iP2	(<i>R</i>)- 2	presesnce ^b	methanol	5.9
SG-sP3	(<i>R</i>)- 3	absence	methanol	6.2
SG-iP3	(<i>R</i>)- 3	presesnce	methanol	8.3
SG-sP4	(<i>R</i>)- 4	absence	methanol	6.2
SG-iP4	(<i>R</i>)- 4	presesnce	methanol	12.1
SG-sP5	(-)- 5	absence	chloroform	13.9
SG-iP5	(-)- 5	presesnce	chloroform	14.7

^aMonomer = 0.5 g, **6** = 1.0 g, solvent = 1.6–2.1 mL, [monomer]₀/[AIBN]₀ = 50, temp. = 60 °C, time = 24 hr. ^b[Yb(OTf)₃]₀/[monomer]₀ = 0.1). ^cEstimated by TG.

Table IV. Capacity (*k'*) and separation factors (α) for eight racemates (**7–14**) on poly[(*R*)-**2**]s and poly[(*R*)-**3**]s immobilized on silica gel^a

Racemate	Packing material	SG-sP2		SG-iP2		SG-sP3		SG-iP3	
		<i>k</i> ₁ '	α	<i>k</i> ₁ '	α	<i>k</i> ₁ '	α	<i>k</i> ₁ '	α
7		0.89	1.00	1.09(–)	1.11	0.58	1.00	0.72	1.00
8		0.25	1.00	0.12	1.00	0.22	1.00	0.25	1.00
9		1.28(–)	1.08	2.13(–)	1.14	5.37	~1	2.68	~1
10		not eluted		6.25	1.00	not eluted		5.45(+) ^b	1.61
11		3.53(+)	1.19	0.95(+)	~1	3.19(–)	1.42	2.21(–)	1.14
12		2.92(+) ^c	1.21	1.99(+)	1.20	7.73(–)	1.22	1.34(–)	1.19
13		0.17	1.00	0.03	1.00	0.12	1.00	0.13	1.00
14		0.42	1.00	0.10	1.00	0.28	1.00	0.18	1.00

^aFlow rate = 0.1 mL/min, column = 2.0 mm (i.d.) × 250 mm, eluent = hexane/chloroform/2-propanol (90/10/1). The sign of the optical rotation of the first-eluted isomer is shown as (+) or (–). ^bFlow rate = 0.3 mL/min. ^cEluent = hexane/2-propanol (90/10).

Table V. Capacity (*k'*) and separation factors (α) for eight racemates (**7–14**) on poly[(*R*)-**4**]s and poly[(-)-**5**]s immobilized on silica gel^a

Racemate	Packing material	SG-sP4 ^b		SG-iP4 ^b		SG-sP5 ^c		SG-iP5 ^c	
		<i>k</i> ₁ '	α	<i>k</i> ₁ '	α	<i>k</i> ₁ '	α	<i>k</i> ₁ '	α
7		0.71(–)	~1	1.42	1.00	2.13	1.00	0.68	1.00
8		0.27	1.00	0.27	1.00	1.19	1.00	0.53(–)	~1
9		3.62	1.13	2.29	1.14	1.72	1.08	0.95	~1
10		0.54(–) ^c	1.39	0.32 ^c	1.00	0.94(–)	1.27	0.61(–)	1.30
11		2.17(–)	1.28	1.04	1.00	5.81(+)	1.45	1.03(+)	~1
12		8.82(–)	1.34	3.13(–)	1.13	5.94(+)	1.43	2.53(+)	1.24
13		0.17	1.00	0.17	1.00	0.42	1.00	0.34	1.00
14		0.27	1.00	0.27	1.00	0.78(+)	1.88	0.34(+)	1.71

^aFlow rate = 0.1 mL/min, column = 2.0 mm (i.d.) × 250 mm. ^bEluent = hexane/chloroform/2-propanol (90/10/1). ^cEluent = hexane/2-propanol (90/10).

t_0 , t_1 , and t_2 are the dead time of a column, the elution time of the first-eluted isomer, and that of the second-eluted isomer, respectively. In the tables, the sign of the optical rotation of the first-eluted isomer is shown as (+) or (–). The separation factor (α), which reflects the chiral recognition ability of a CSP, can be estimat-

ed as k_2'/k_1' . A typical chromatogram of the resolution of **14** on SG-sP5 monitored by UV and polarimetric detectors is shown in Figure 7. The CSPs showed chiral recognition for the compounds having polar groups, such as hydroxyl and amide groups. As an eluent, hexane/2-propanol (90/10 (v/v)) or hexane/

Figure 7. HPLC separation of enantiomer **14** on SG-sP5 [Conditions: flow rate = 0.1 mL/min, column = 20 mm (i.d.) $\times$ 250 nm, eluent = hexane/2-propanol (90/10)].

chloroform/2-propanol (90/10/1 (v/v/v)) was used. The chiral recognition was clearly affected by the stereoregularity of the immobilized poly(methacrylamide)s, although the elution order of the enantiomers remained the same. For example, racemate **7** was not separated on the CSPs with the syndiotactic poly[(*R*)-**2**] (SG-sP2) and other poly(methacrylamide)s, but the CSP with the isotactic poly[(*R*)-**2**] (SG-iP2) resolved it. On the other hand, the syndiotactic poly[(*R*)-**4**] (SG-sP4) indicated higher resolving abilities for **10**, **11**, and **12** than the isotactic poly[(*R*)-**4**] (SG-iP4). The syndiotactic poly[(*−*)-**5**] showed a higher α value for **9**, **11**, **12**, and **14** than the isotactic polymer (SG-iP5). The k_1' represents the interaction strength between a CSP and a racemate. The CSPs of syndiotactic polymers indicated a higher k_1' for most racemates than the isotactic polymers. This is ascribed to the fact that the syndiotactic polymers can more efficiently interact with polar racemates through

hydrogen-bonding. These results agree with the fact that the isotactic polymethacrylamides can form more efficient intramolecular hydrogen-bonds than the syndiotactic polymers.

NMR Study on Interaction of Poly[(*R*)-**3**]s with **12**

The ^1H NMR measurement of the mixture of poly[(*R*)-**3**]s and racemic **12** was carried out in chloroform-*d* (Figure 8). The hydroxyl peak of **12** was split into two peaks due to the (+)- and (−)-enantiomers through the interaction between poly[(*R*)-**3**] and the racemate. The peak of the (+)-enantiomer, shifted to lower magnetic field than the (−)-isomer. The shift was more significant for the syndiotactic poly[(*R*)-**3**] obtained by the conventional polymerization than the isotactic one prepared in the presence of Yb(OTf)₃. Although a large change in chemical shift does not always mean a stronger interaction, from the results of the HPLC separation, the larger shift by the syndiotactic polymer appears to be associated to the its stronger interaction with (+)-isomer.

CONCLUSIONS

The radical polymerization of the optically active methacrylamides was performed under various conditions using Lewis acids, such as Yb(OTf)₃ and Y(OTf)₃. Although the conventional polymerization without Lewis acid produced syndiotactic polymers, isotactic-rich polymers were obtained in the presence of the Lewis acids. The tacticity influenced the intramolecular hydrogen bond formation, the higher order structure, and the chiral recognition ability. The polymethacrylamides having different tacticities were immobilized on silica gel and used as the CSPs for HPLC resolution of the various racemates.

Figure 8. ^1H NMR spectra of the hydroxyl proton resonances of 1,1'-bi-2-naphthol (**12**) (3.66 mmol/L) in the absence (a) and presence of poly[(*R*)-**3**] (7.39 mmol/L (monomer residue)) obtained in the absence of Yb(OTf)₃ (b) and poly[(*R*)-**3**] obtained in the presence of Yb(OTf)₃ (c) in CDCl₃ at 23 °C.

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