

Syntheses and Polymerizations of Novel Chiral Methacrylates Bearing Urethane Bonds and *N, N*-Dibenzylamino Groups

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ABSTRACT: Four new chiral methacrylates bearing urethane bonds and *N, N*-dibenzylamino groups (RMOC) were synthesized from 2-methacryloyloxyethyl isocyanate (MOI) and four chiral alcohol derivatives of α -amino acids, L-valine, L-leucine, D-phenylglycine, and L-phenylalanine. Radical polymerizations of RMOC were performed under various conditions to obtain the corresponding poly(RMOC) with number average molecular weights (M_n) of 2.4×10^4 – 6.4×10^4 . Poly(RMOC) has hydrogen bonds based on urethane segments in solvent and exhibited negative (levo) rotation. Specific optical rotations of poly(RMOC) were slightly influenced by solvent and temperature. Radical copolymerizations of RMOC with styrene (ST) and methyl methacrylate (MMA) were performed with AIBN in toluene at 60 °C. Monomer reactivity ratios (r_1, r_2) and Alfrey–Price $Q-e$ were determined. Chiroptical properties of the copolymers were scarcely affected by *co*-units of ST and MMA. Chiral stationary phases (CSPs) for high performance liquid chromatography (HPLC) were prepared from poly(RMOC) and silica gel and optical resolution ability was investigated. CSPs resolved some racemic compounds (1–5) using methanol/water as mobile phase.

KEY WORDS 2-Methacryloyloxyethyl Isocyanate / Radical Polymerization / Copolymerization / Monomer Reactivity Ratios / Chiral Stationary Phase / High Performance Liquid Chromatography /

2-Methacryloyloxyethyl isocyanate (MOI) is a difunctional monomer with a reactive isocyanate group and polymerizable double bond.¹ Many MOI derivatives have been synthesized from several alcohols and amines, and polymerized.² MOI is useful for preparation of macromonomer.³ However there have been few reports on the synthesis of MOI derivatives bearing optically active groups. Kamogawa *et al.*^{2a} synthesized and polymerized *l*-menthyl *N*-(2-methacryloyloxyethyl)carbamate (MnMOC) and investigated the utilization of hydrolytic properties of various bonds between the monomer and polymer. Bamford *et al.*⁴ synthesized MOI derivatives from α -amino acid and D-glucosamine and examined applications of polymers to blood compatibility. To our knowledge, no chiroptical properties of MOI derivatives with optically active groups have been reported. Thus, the authors lately investigated polymerizations and chiroptical properties of cholesteryl *N*-(2-methacryloyloxyethyl)carbamate (ChMOC) and MnMOC.⁵

A wide variety of chiral stationary phases (CSPs) has recently been developed for the separation of enantiomers by high performance liquid chromatography (HPLC).⁶ Although many synthetic chiral polymers were applied to CSPs,⁷ there have been few reports on the preparation of CSPs for HPLC from polymethacrylate bearing a chiral pendant group in spite of their availability. Only Miyano *et al.*⁸ synthesized optically active polymethacrylates each bearing a 1,1'-binaphthalene moiety as pendant group and investigated on optical resolution ability as chiral adsorbent for HPLC. The reason may be the low chiral recognition ability of the chiral pendant group and/or the absence of the stable higher-ordered structure of the polymers.⁷ However, methacrylamides bearing a chiral pendant groups served as CSPs with highly recognition ability. Blaschke *et al.*⁹ and Arlt *et*

*al.*¹⁰ reported the synthesis of many chiral methacrylamides from α -amino acids and their chiral recognition ability.

This article describes the synthesis of four new chiral methacrylate (RMOC) with urethane bonds and α -amino acids derivatives, and radical homopolymerizations, copolymerizations, and chiroptical properties of the polymers obtained. CSPs were prepared by chemical reaction of silica gel and poly(RMOC). Optical resolution ability of the CSPs was investigated by HPLC.

EXPERIMENTAL

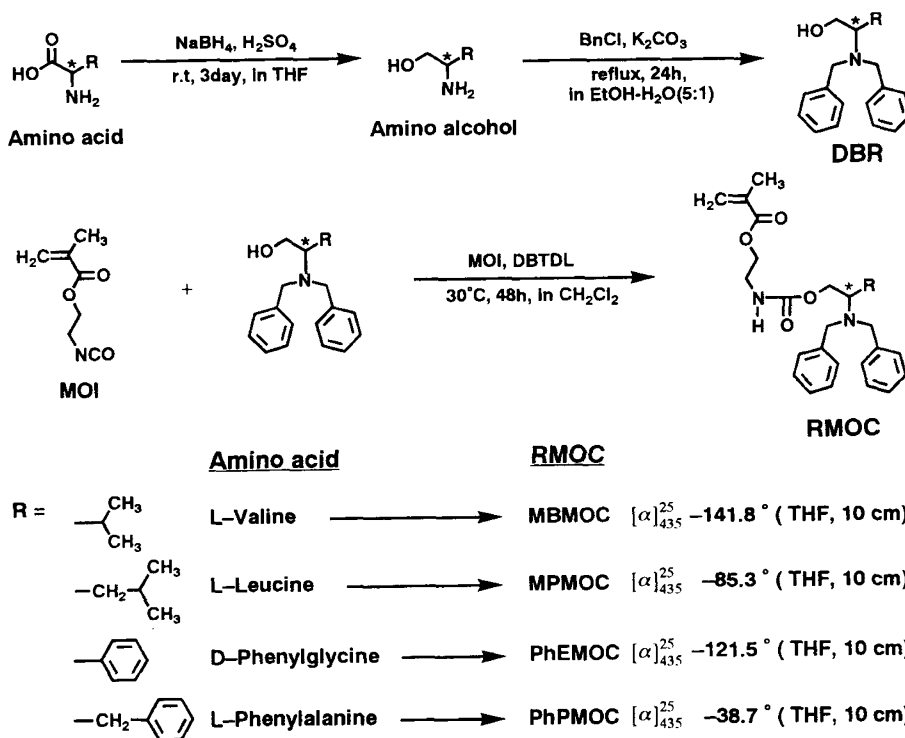
Materials

Styrene (ST) and methyl methacrylate (MMA) were purified by ordinary methods.¹¹ Tetrahydrofuran (THF), benzene, and toluene were dried over sodium metal and used after distillation. *N, N*-Dimethylformamide (DMF), dichloromethane, and chloroform were used after distillation. 2,2'-Azobisisobutyronitrile (AIBN) was purified by recrystallization from methanol. Other reagents were used without further purification. Monomers of RMOC were synthesized, as drawn in Scheme 1.

Amino Alcohols. Four amino alcohols, (*S*)-valinol, (*S*)-leucinol, (*R*)-phenylglycinol, and (*S*)-phenylalaninol, were synthesized from L-valine, L-leucine, D-phenylglycine, and L-phenylalanine, respectively, by the ordinary methods.¹²

(*S*) and (*R*)-2-(*N, N*-Dibenzylamino)-substituted-1-ol (DBR). (*S*)-2-(*N, N*-Dibenzylamino)-3-methylbutane-1-ol (DBMB), (*S*)-2-(*N, N*-dibenzylamino)-4-methylpentane-1-ol (DBMP), (*R*)-2-(*N, N*-dibenzylamino)-2-phenylethane-1-ol (DBPhE), and (*S*)-2-(*N, N*-dibenzylamino)-3-phenylpropane-1-ol (DBPhP) were synthesized from (*S*)-valinol, (*S*)-leucinol, (*R*)-phenylglycinol, and (*S*)-phenylalaninol, re-

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Scheme 1.

spectively, by ordinary methods.¹³

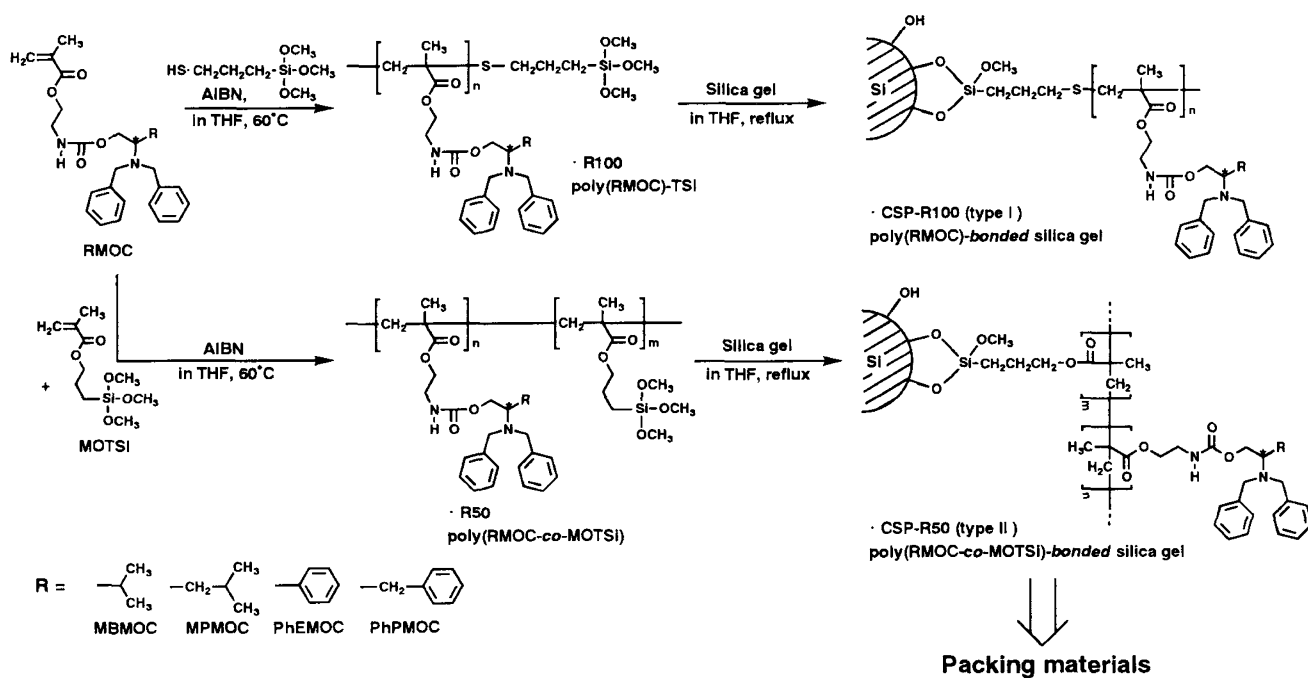
(*S*)-(2-(*N,N*-Dibenzylamino)-3-methyl)butyl *N*-(2-methacryloyloxyethyl) carbamate (MBMOC). A solution of MOI (1.97 g, 1.27×10^{-2} mol) was added dropwise to a stirred solution of DBMB (3.01 g, 1.06×10^{-2} mol) and di-*n*-butyltin dilaurate (DBTDL) (0.01 g, 1.58×10^{-5} mol) in CH_2Cl_2 (30 mL) under nitrogen at r.t. The solution was heated at 35°C and stirred for 48 h under nitrogen. The reaction mixture was extracted with distilled water. The organic layer was dried with anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure to give the crude product. Purification by chromatography on silica gel with *n*-hexane / ethyl acetate (4 / 1) as eluent gave MBMOC as a pale yellow viscous oil: yield 67.1%; $[\alpha]_{435}^{25} -141.8^\circ$ ($c = 1.0 \text{ g dL}^{-1}$, $l = 10 \text{ cm}$, THF); $^1\text{H NMR}$ (δ , ppm from TMS in CDCl_3) 7.37–7.18 (m, 10H, in phenyl groups), 6.13 (s, 1H, (*trans*) $\text{CH}_2=\text{C}$), 5.59 (s, 1H, (*cis*) $\text{CH}_2=\text{C}$), 4.95 (bs, 1H, N-H), 4.44–4.39 (dd, 2H, $J = 3.68$ and 8.25 , $2 \times \text{PhCH}_A\text{H}_B\text{N}$), 4.29–4.25 (t, 2H, $J = 5.28$, COOCH_2), 3.90–3.85 (d, 2H, $J = 3.85$, $2 \times \text{PhCH}_A\text{H}_B\text{N}$), 3.56–3.48 (m, 4H, $\text{CH}_2\text{NHCOOCH}_2$), 2.45–2.38 (m, 1H, CH-N), 1.95 (bs, 4H, $\text{CH}(\text{CH}_3)_2$ and $\text{CH}_2=\text{C}(\text{CH}_3)$), 1.03–0.84 (dd, 6H, $J = 6.60$, $\text{CH}(\text{CH}_3)_2$); $^{13}\text{C NMR}$ (δ , ppm from TMS in CDCl_3) 167.76 (C=O), 156.84 (N-C=O), 140.61, 129.36, 128.57, 127.22 (in phenyl groups), 136.41 (=C<), 126.52 ($\text{CH}_2=$), 64.10 (NHCOOCH_2), 63.00 (COOCH_2), 62.50 (N-CH), 55.01 (PhCH_2N), 40.72 (CH_2NHCOO), 28.38 ($\text{CH}(\text{CH}_3)_2$), 21.58, 20.70 ($\text{CH}(\text{CH}_3)_2$), 18.76 ($\text{CH}_2=\text{C}(\text{CH}_3)$).

(*S*)-(2-(*N,N*-Dibenzylamino)-4-methyl)pentyl *N*-(2-methacryloyloxyethyl) carbamate (MPMOC), (*R*)-(2, 2'-(*N,N*-Dibenzylamino)phenyl)ethyl *N*-(2-methacryloyloxyethyl)carbamate (PhEMOC), and (*S*)-(2-(*N,N*-Dibenzylamino)-3-phenyl)propyl *N*-(2-methacryloyloxyethyl)carbamate (PhPMOC) were synthesized from DBMB,

DBPhE, and DBPhP, respectively, by the same procedure as for MBMOC.

MPMOC. Yield 64.7% $[\alpha]_{435}^{25} -85.3^\circ$ ($c = 1.0 \text{ g dL}^{-1}$, $l = 10 \text{ cm}$, THF); $^1\text{H NMR}$ (δ , ppm from TMS in CDCl_3) 7.36–7.16 (m, 10H, in phenyl groups), 6.12 (s, 1H, (*trans*) $\text{CH}_2=\text{C}$), 5.57 (s, 1H, (*cis*) $\text{CH}_2=\text{C}$), 5.11 (bs, 1H, N-H), 4.48–4.05 (m, 4H, $2 \times \text{PhCH}_A\text{H}_B\text{N}$ and COOCH_2), 3.73–3.52 (m, 6H, $2 \times \text{PhCH}_A\text{H}_B\text{N}$ and $\text{CH}_2\text{NHCOOCH}_2$), 3.50–3.45 (m, 1H, CH-N), 1.93 (s, 3H, CH_3), 1.78–1.42 (dm, 1H, $\text{CH}_A\text{H}_B\text{CH}(\text{CH}_3)_2$), 1.26–1.20 (m, 1H, $\text{CH}_A\text{H}_B\text{CH}(\text{CH}_3)_2$), 1.15–0.77 (dm, 1H, $\text{CH}_A\text{H}_B\text{CH}(\text{CH}_3)_2$), 0.84–0.61 (dd, 6H, $J = 6.60$, $\text{CH}_A\text{H}_B\text{CH}(\text{CH}_3)_2$); $^{13}\text{C NMR}$ (δ , ppm from TMS in CDCl_3) 167.22 (C=O), 156.41 (N-C=O), 140.2, 128.82, 128.25, 126.74 (in phenyl groups), 135.90 (=C<), 125.97 ($\text{CH}_2=$), 64.96 (NHCOOCH_2), 63.61 (COOCH_2), 53.95 (N-CH), 53.82 (PhCH_2N), 40.18 (CH_2NHCOO), 37.65 ($\text{CH}_2\text{CH}(\text{CH}_3)_2$), 24.85 ($\text{CH}_2\text{CH}(\text{CH}_3)_2$), 23.24, 22.23 ($\text{CH}_2\text{CH}(\text{CH}_3)_2$), 18.24 (CH_3).

PhEMOC. Yield 98.7%; $[\alpha]_{435}^{25} -121.5^\circ$ ($c = 1.0 \text{ g dL}^{-1}$, $l = 10 \text{ cm}$, THF); $^1\text{H NMR}$ (δ , ppm from TMS in CDCl_3) 7.42–7.19 (m, 15H, in phenyl groups), 6.10 (s, 1H, (*trans*) $\text{CH}_2=\text{C}$), 5.58 (s, 1H, (*cis*) $\text{CH}_2=\text{C}$), 4.89 (bs, 1H, N-H), 4.73–4.66 (dd, 1H, $J = 4.29$ and 6.93 , $\text{PhCH}_A\text{H}_B\text{N}$), 4.50–4.43 (dd, 1H, $J = 3.63$ and 7.25 , $\text{PhCH}_A\text{H}_B\text{N}$), 4.24–4.20 (t, 2H, $J = 5.28$, COOCH_2), 4.07–4.02 (t, 1H, $J = 6.92$, CH-N), 3.82–3.77 (d, 2H, $J = 3.86$, $2 \times \text{PhCH}_A\text{H}_B\text{N}$), 3.49–3.47 (d, 2H, $J = 4.62$, CH_2NHCOO), 3.36–3.31 (d, 2H, $J = 3.53$, NHCOOCH_2), 1.93 (s, 3H, CH_3); $^{13}\text{C NMR}$ (δ , ppm from TMS in CDCl_3) 167.24 (C=O), 156.26 (N-C=O), 139.75, 129.06, 128.75, 128.70, 128.23, 128.18, 127.48, 126.92 (in phenyl groups), 135.92 (=C<), 126.04 ($\text{CH}_2=$), 63.63 (COOCH_2 and NHCOOCH_2), 60.40 (N-CH), 54.05 (PhCH_2N), 40.16 (CH_2NHCOO), 18.28 (CH_3).



Scheme 2.

PhPMOC. Yield 63.0%; $[\alpha]_{435}^{25} - 38.7^\circ$ ($c = 1.0 \text{ g dL}^{-1}$, $l = 10 \text{ cm}$, THF); $^1\text{H NMR}$ (δ , ppm from TMS in CDCl_3) 7.23–7.03 (m, 15H, in phenyl groups), 6.12 (s, 1H, (*trans*) $\text{CH}_2=\text{C}$), 5.57 (s, 1H, (*cis*) $\text{CH}_2=\text{C}$), 4.95 (bs, 1H, N–H), 4.33–4.07 (m, 4H, $2 \times \text{PhCH}_A\text{H}_B\text{N}$ and COOCH_2), 3.72 (bs, 4H, $2 \times \text{PhCH}_A\text{H}_B\text{N}$ and NHCOOCH_2), 3.51–3.45 (d, 2H, $J = 5.28$, CH_2NHCOO), 3.20–3.16 (m, 1H, CH–N), 3.00–2.92 (dd, 1H, $J = 6.60$ and 6.93 , PhCH_AH_B), 2.72–2.64 (dd, 1H, $J = 5.94$ and 7.59 , PhCH_AH_B), 1.93 (s, 3H, CH_3); $^{13}\text{C NMR}$ (δ , ppm from TMS in CDCl_3) 167.21 (C=O), 156.24 (N–C=O), 139.77, 139.46, 129.20, 128.91, 128.54, 128.46, 128.19, 128.05, 126.15, 125.98 (in phenyl groups), 135.89 (=C<), 125.95 ($\text{CH}_2=$), 64.19 (NHCOOCH_2), 63.58 (COOCH_2), 58.26 (N–CH), 53.17 (PhCH_2N), 40.15 (CH_2NHCOO), 34.34 (PhCH_2), 18.22 (CH_3).

Radical Polymerization

Radical homopolymerization and copolymerization were performed with AIBN as initiator in a suitable solvent in a sealed tube at 60°C . After polymerization, the polymer solution was poured into excess methanol to precipitate the polymer. The resulting polymer was purified by reprecipitating it twice from THF solution into excess methanol. The supernatant was decanted and the polymer dried *in vacuo* for 3 days. The compositions of copolymers were found from $^1\text{H NMR}$ spectra and elemental analysis (N).

Preparation of Packing Materials and Column Packing

As shown in Scheme 2, poly(RMOC)s with terminal trimethoxysilane groups (poly(RMOC)-TSi, R100) and poly(RMOC-co-methacryloyloxypropyl trimethoxy silane (MOTSi)) (R50) were synthesized by radical homopolymerization using 3-mercaptopropyl trimethoxysilane as chain-transfer agent and copolymerization with MOTSi, respectively. The chiral polymer (R100 or R50, 0.5 g) was

dissolved in THF (15 mL), and silica gel (TOSOH, TSK-GEL SI 100: mean particle size, $5 \mu\text{m}$; pore size 100 \AA) (1.0 g) was added to the solution. The solution was refluxed for 24 h under nitrogen and cooled to r.t. The solvent was removed by filtration and the polymer-bonded silica gel was washed with THF and methanol and then dried *in vacuo* for 1 day. RMOC segment content on the silica gel obtained was estimated from IR spectra. Chiral packing materials was packed in a stainless steel HPLC column (*i.d.*, 0.2 cm; length, 10 cm) by a slurry method. Plate numbers of columns were measured for toluene in methanol as eluent at a flow rate of 0.5 mL min^{-1} at ambient temperature.

Measurements

NMR spectra were recorded at 25°C using JEOL EX-270 (JEOL Ltd.). IR spectra were recorded on Shimadzu FT-IR-8100 A (Shimadzu Ltd.). Elemental analysis was carried out with a CHN recorder (Yanagimoto Co.). Gel permeation chromatography (GPC) measurements were carried out at 50°C using THF as eluent on a Shimadzu SPD-10 A (Shimadzu Ltd.) equipped with a UV detector, HSG-40, HSG-20, HSG-15, and HSG-10 columns and Jasco OR 990 (Japan Spectroscopic Co.) with a polarimetric detector. Specific optical rotations were measured with a Jasco DIP-140 (5 and 10 cm quartz cell lengths, $c = 1.0 \text{ g dL}^{-1}$ in THF). HPLC measurements were carried out on a Shimadzu LC-10AT with UV detection at 254 nm.

RESULTS AND DISCUSSION

Radical homopolymerizations of RMOC

Radical polymerizations of RMOC were performed with AIBN as initiator at 60°C in various solvents. The results are summarized in Table I. All polymerizations proceeded homogeneously throughout. The obtained

Table I. Radical homopolymerization of RMOC with AIBN in several solvents (2 mL) for 24 h at 60°C^a

Run	Monomer	Polym. solvent	Yield ^b	\bar{M}_n^c	\bar{M}_w/\bar{M}_n^c	$[\alpha]_{435}^{25\text{ d}}$
			%	$\times 10^{-4}$		deg
1	MBMOC	Toluene	85.2	3.30	3.11	-141.0
2		Benzene	79.3	2.98	3.11	-141.3
3		THF	72.9	2.19	3.05	-145.9
4		CHCl ₃	72.9	2.05	2.50	-143.3
5		DMF	69.5	2.59	2.60	-143.0
6	MPMOC	Toluene	85.3	2.97	3.53	-94.3
7		Benzene	84.8	2.74	4.38	-95.6
8		THF	72.5	2.06	3.17	-95.8
9		CHCl ₃	80.3	1.84	3.26	-95.7
10		DMF	73.8	2.43	2.43	-95.4
11	PhMOC	Toluene	89.8	6.73	2.96	-109.0
12		Benzene	82.1	7.12	3.09	-113.4
13		THF	79.6	4.16	2.33	-114.9
14		CHCl ₃	84.7	4.67	2.72	-110.0
15		DMF	85.5	5.75	3.00	-112.2
16 ^e	PhPMOC	Toluene	72.8	3.70	3.23	-42.0
17		Benzene	72.4	3.01	3.95	-43.7
18		THF	55.8	2.18	2.89	-41.4
19		CHCl ₃	60.8	2.09	2.78	-41.5

^a Monomer = 0.5 g; AIBN, 2,2'-azobisisobutyronitrile; [AIBN]/[Monomer] = 0.03. ^b MeOH-insoluble part. ^c By GPC. ^d $c = 1.0 \text{ g dL}^{-1}$, $l = 10 \text{ cm}$, THF. ^e Monomer = 1.0 g; toluene = 5 mL; [AIBN]/[Monomer] = 0.08.

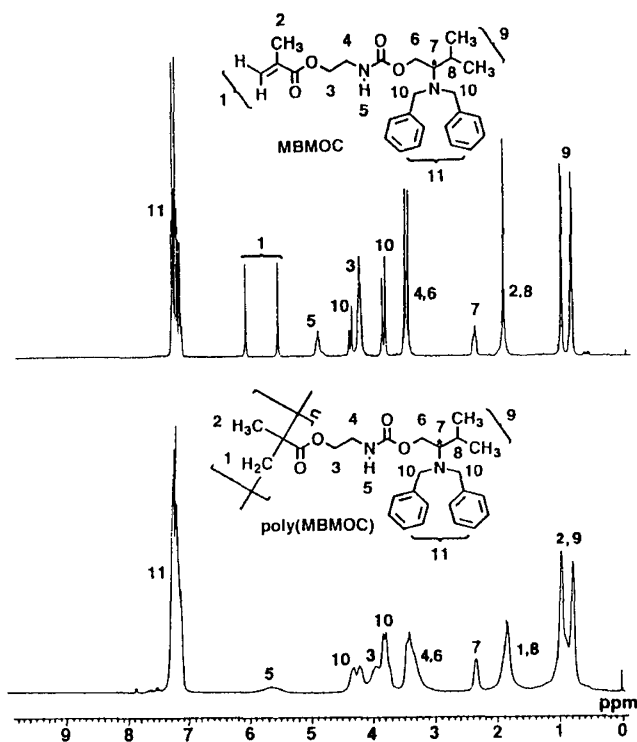


Figure 1. ¹H NMR spectra for MBMOC and poly(MBMOC) in CDCl₃ at 23.5°C (270 MHz).

polymers were colorless or pale yellow powders, though sticky and rubbery in methanol and *n*-hexane. The resulting polymers were soluble in organic solvents such as THF, chloroform, and benzene. Poly(RMOC) showed counterdextro specific optical rotations ($[\alpha]_{435}^{25}$) of -41.4 — -145.9°. Chiroptical properties of the polymers will be described later. Figure 1 shows ¹H NMR spectra of MBMOC and poly(MBMOC). Peaks at 6.13 ppm and 5.59 ppm assigned to vinyl (CH₂=C<) groups disappeared and those due to carbamate (-NHCOO-) groups

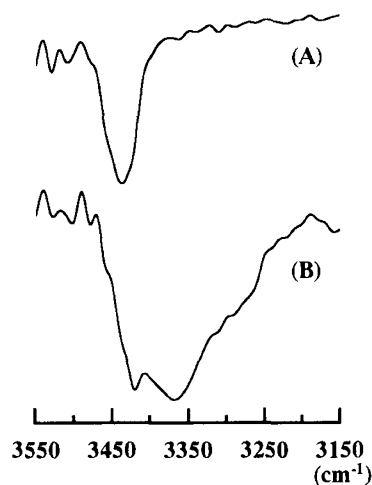


Figure 2. Infrared spectra for (A) PhMOC and (B) poly(PhMOC) in benzene; $c = 1.0 \text{ g dL}^{-1}$.

at 4.95 ppm became broad and shifted to 5.70 ppm after polymerization, suggesting that ordinary vinyl radical polymerization completely proceeded. Expanded IR spectra of PhMOC and poly(PhMOC) measured in benzene are shown in Figure 2. A sharp absorption peak due to stretching vibration of N-H for PhMOC appeared at 3440 cm⁻¹. For poly(PhMOC), the peak shifted from 3440 cm⁻¹ to 3365 cm⁻¹ and became broad, suggesting that the polymers had hydrogen bonds based on urethane segments. For other poly(RMOC)s, similar results were observed. Figure 3 shows ¹H NMR spectra of poly(MBMOC) measured at various temperatures and concentrations. With increasing temperature, the broad peak due to carbamate groups at 5.70 ppm shifted slightly to the high magnetic field, as well as the peak due to methylene groups adjacent to the carbamate groups at 3.42 ppm. However, such chemical shift was not observed by changing concentration. The polymer

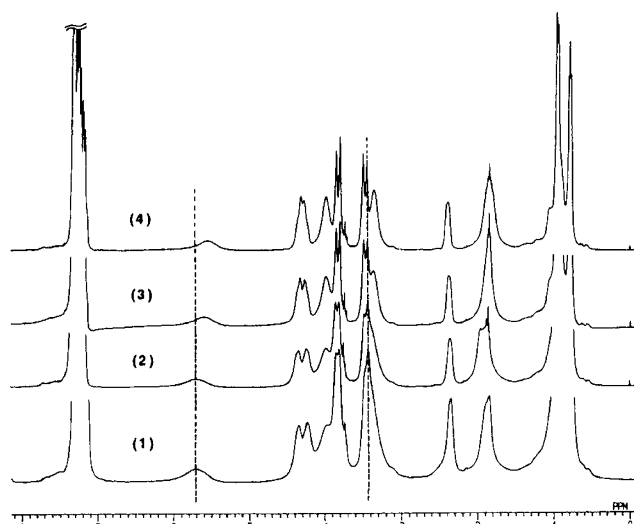


Figure 3. ^1H NMR spectra for MBMOC and poly(MBMOC) in CDCl_3 at (1) 23.2°C ($c=2.0\text{ g dL}^{-1}$), (2) 23.2°C ($c=0.75\text{ g dL}^{-1}$), (3) 40°C ($c=0.75\text{ g dL}^{-1}$), and 50°C ($c=0.75\text{ g dL}^{-1}$).

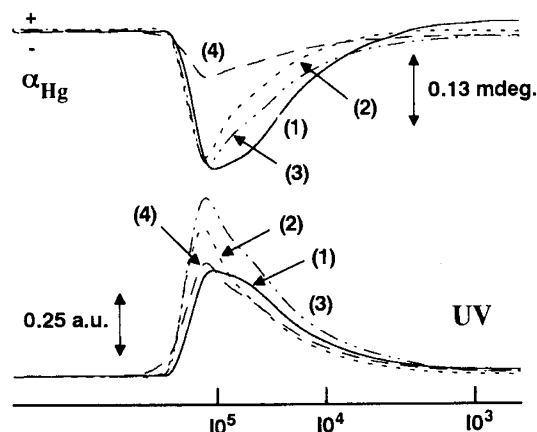


Figure 4. GPC curves of poly(RMOC): (1) run 3, (2) run 7, (3) run 13, and (4) run 16 in Table I.

Table II. Radical Copolymerizations of RMOC (M_1) with ST (M_2) in Toluene (2 mL) at 60°C ^a

Run	M_1	M_2	M_1 in		Polym. time h	Yield ^b %	M_1 in		\overline{M}_n ^d $\times 10^{-4}$	$\overline{M}_w/\overline{M}_n$ ^b	$[\alpha]_{435}^{25}$ ^e deg
			monomer feed mol%	mol%			wt%				
1	MBMOC	ST	9.8	9.8	12.0	33.4	20.1	51.4	1.30	1.68	-63.2
2		ST	19.9	19.9	11.0	34.6	31.5	66.0	1.44	1.71	-91.1
3		ST	30.0	30.0	8.0	18.1	44.6	77.2	1.92	1.73	-105.4 ^f
4		ST	48.8	48.8	7.0	26.3	61.7	87.1	2.14	1.88	-120.9
5		ST	69.7	69.7	4.0	12.0	69.3	90.5	3.27	2.03	-132.4 ^g
6		ST	79.5	79.5	2.5	20.2	83.7	95.6	3.55	2.17	-136.9 ^h
7	MPMOC	ST	10.2	10.2	9.0	13.8	14.4	42.3	1.37	1.67	-41.5 ⁱ
8		ST	20.3	20.3	9.0	24.3	23.5	57.2	1.72	1.73	-58.1
9		ST	30.2	30.2	6.0	8.5	31.1	66.3	2.01	1.76	-67.6 ^g
10		ST	50.1	50.1	5.5	22.8	67.5	90.0	2.28	2.00	-82.2 ^h
11		ST	79.1	79.1	3.5	21.3	70.9	91.0	3.48	2.10	-86.5
12	PhEMOC	ST	9.1	9.1	5.5	7.3	18.8	51.2	1.51	1.86	-50.0 ^j
13		ST	20.8	20.8	5.5	5.0	35.6	71.5	1.80	1.80	-72.2 ^k
14		ST	24.3	24.3	5.0	6.6	38.1	73.6	1.78	1.89	-76.8 ^l
15		ST	47.5	47.5	4.5	6.2	62.8	88.5	2.28	2.12	-89.5 ^l
16		ST	68.5	68.5	4.0	10.0	75.6	93.4	2.39	2.13	-96.6 ^l
17		ST	81.6	81.6	3.5	18.2	88.9	97.3	3.00	2.30	-101.2 ^m
18	PhPMOC	ST	10.5	10.5	9.5	14.7	21.1	55.6	1.27	1.86	-22.5 ^m
19		ST	20.9	20.9	9.5	20.7	33.1	69.8	1.38	2.05	-29.4 ^m
20		ST	30.1	30.1	9.5	29.3	40.2	75.9	1.62	2.37	-31.8
21		ST	48.2	48.2	7.0	11.4	58.6	86.9	— ⁿ	— ⁿ	— ⁿ
22		ST	69.5	69.5	5.0	15.4	66.4	90.2	2.54	3.75	-38.5 ^m
23		ST	79.5	79.5	3.5	10.5	88.0	97.2	3.58	3.69	-38.5 ^m

^a $M_1 + M_2 = 0.5\text{ g}$; initiator, 2,2'-azobisisobutyronitrile (0.03 mol L^{-1}). ^b Methanol insoluble part. ^c By elemental analysis. ^d By GPC with polystyrene standard. ^e $c=1.0\text{ g dL}^{-1}$, $l=10\text{ cm}$, THF. ^f $c=0.7\text{ g dL}^{-1}$, $l=10\text{ cm}$, THF. ^g $c=0.4\text{ g dL}^{-1}$, $l=10\text{ cm}$, THF. ^h $c=0.8\text{ g dL}^{-1}$, $l=10\text{ cm}$, THF. ⁱ $c=0.5\text{ g dL}^{-1}$, $l=10\text{ cm}$, THF. ^j $c=0.4\text{ g dL}^{-1}$, $l=5\text{ cm}$, THF. ^k $c=0.36\text{ g dL}^{-1}$, $l=5\text{ cm}$, THF. ^l $c=0.8\text{ g dL}^{-1}$, $l=5\text{ cm}$, THF. ^m $c=1.0\text{ g dL}^{-1}$, $l=5\text{ cm}$, THF. ⁿ Not determined.

may thus have intra- rather than intermolecular hydrogen bonds based on urethane segments.

Figure 4 depicts GPC curves of poly(RMOC)s. Number-average molecular weights (\overline{M}_n) of poly(RMOC)s were 1.84×10^4 – 7.12×10^4 , and slightly affected by polymerization solvents. \overline{M}_n of poly(PhEMOC) was larger than those of other polymers. Polydispersities (weight average molecular weight ($\overline{M}_w/\overline{M}_n$)) for poly(RMOC)s were 2.33–4.38 and relatively large. Yields of poly(RMOC)s were 55.8–89.8% and influenced only by polymerization solvents.

Radical copolymerizations of RMOC with ST and MMA

The results of radical copolymerizations of RMOC (M_1) with ST (M_2) or MMA (M_2) using AIBN in toluene at 60°C are summarized in Tables II and III. All copolymerizations proceeded homogeneously throughout. The copolymers were colorless or pale yellow powders and optically active. \overline{M}_n s of poly(RMOC-co-ST)s and poly(RMOC-co-MMA)s were 1.27×10^4 – 3.58×10^4 and 2.51×10^4 – 7.45×10^4 , respectively. \overline{M}_n s of all copolymers increased with the content of M_1 in the copolymer. ($\overline{M}_w/\overline{M}_n$)s for the copolymers were 1.67–6.74 and comparatively

Table III. Radical Copolymerizations of RMOC (M_1) with MMA (M_2) in Toluene (2 mL) at 60 °C ^a

Run	M_1	M_2	M_1 in	Polym. time	Yield ^b	M_1 in		\overline{M}_n ^d	$\overline{M}_w/\overline{M}_n$ ^b	$[\alpha]_{435}^{25}$ ^e
			monomer feed			copolymer ^c	$\times 10^{-4}$			
			mol%	h	%	mol%	wt%			
1	MBMOC	MMA	10.0	3.5	40.8	13.2	39.9	4.28	1.86	-51.0
2		MMA	29.9	2.5	40.9	32.4	67.7	4.52	2.54	-94.1
3		MMA	47.4	1.5	40.2	49.7	81.2	5.96	3.01	-110.5
4		MMA	69.4	1.0	45.8	60.5	87.0	6.53	3.10	-123.5
5		MMA	78.9	1.0	54.2	79.8	94.5	6.49	3.20	-129.9
6	MPMOC	MMA	10.1	2.0	29.7	12.0	38.2	4.56	2.24	-35.7
7		MMA	19.3	1.5	22.6	23.2	57.7	4.81	2.40	-53.8
8		MMA	29.8	1.5	28.0	33.2	69.2	4.86	2.46	-66.3
9		MMA	50.2	1.0	27.4	52.3	83.2	5.49	2.77	-81.2
10		MMA	68.9	1.0	31.3	66.0	89.8	6.56	3.15	-90.0
11		MMA	78.6	0.5	32.3	89.0	97.3	6.86	3.25	-92.4
12	PhEMOC	MMA	10.6	5.5	47.7	12.3	39.8	3.52	2.45	-42.0
13		MMA	20.3	5.0	58.0	19.7	53.7	3.43	2.48	-61.8
14		MMA	30.5	4.0	56.4	25.4	61.6	3.86	3.08	-76.5
15		MMA	48.3	2.0	41.3	42.7	77.9	5.54	3.14	-89.5
16		MMA	69.8	1.5	41.9	58.7	87.0	6.46	3.33	-99.9
17		MMA	77.4	1.0	37.9	88.8	97.4	7.45	3.32	-101.9
18		PhPMOC	MMA	10.6	4.0	41.2	14.2	44.7	2.51	3.85
19	MMA		19.7	3.5	53.5	27.9	65.3	2.64	4.26	-26.1
20	MMA		29.7	2.5	40.5	35.3	72.6	3.00	5.38	-30.1
21	MMA		51.6	1.5	37.3	50.7	83.4	4.17	6.74	-35.4
22	MMA		69.7	1.0	33.3	71.4	92.4	6.27	4.17	-37.6
23	MMA		78.8	1.0	24.0	87.0	97.0	6.25	3.66	-38.7

^a $M_1 + M_2 = 0.5$ g; initiator, 2,2'-azobisisobutyronitrile (0.03 mol L⁻¹). ^b Methanol insoluble part. ^c By elemental analysis. ^d By GPC with polystyrene standard. ^e $c = 1.0$ g dL⁻¹, $l = 10$ cm, THF.

Table IV. Monomer Reactivity Ratios (r_1, r_2) and Alfrey-Price Q - e values

M_1	M_2	r_1	r_2	Q_1	e_1	Reference
MBMOC	ST	0.99	0.30	1.39	0.30	this work
MPMOC	ST	0.52	0.48	0.81	0.38	this work
PhEMOC	ST	1.33	0.38	1.37	0.03	this work
PhPMOC	ST	1.14	0.38	1.27	0.12	this work
ChMOC	ST	0.38	0.42	0.80	0.55	5
MnMOC	ST	0.41	0.52	0.72	0.45	5
MBMOC	MMA	0.64	0.61	1.80	1.37	this work
MPMOC	MMA	0.76	0.70	1.45	1.19	this work
PhEMOC	MMA	0.69	0.74	1.38	1.22	this work
PhPMOC	MMA	1.15	0.56	1.74	1.07	this work
ChMOC	MMA	0.99	0.83	1.07	0.84	5
MnMOC	MMA	0.45	0.73	1.54	1.45	5

large.

Copolymer composition curves in the polymerizations of RMOC with ST or MMA are shown in Figure 5. Table IV gives monomer reactivity ratios (r_1, r_2) obtained by the high-conversion method reported by Tüdös *et al.*¹⁴ and Alfrey-Price Q - e ¹⁵ for RMOC. Figure 4 and Table IV show that copolymerization systems of RMOC with ST or MMA have similar reactivities. Q_1 and e_1 in the RMOC-ST system were different from those in the RMOC-MMA system. In the Alfrey-Price Q and e theory, no steric effect is taken into account. RMOCs may have possibly relatively high steric hindrance because of a large N, N -dibenzylamino group. These copolymerization parameters were similar to those for other RMOC copolymers.⁵

Chiroptical Properties of Homopolymers and Copolymers

Poly(RMOC)s exhibited negative (levo) specific optical rotations as well as the corresponding monomers. In Figure 4, GPC curves for poly(RMOC)s taken with a po-

larimetric detector also show negative peaks, whose patterns were in accord with the corresponding UV curves. Thus chiroptical properties of poly(RMOC)s were not affected by \overline{M}_n . Specific optical rotations of the polymers were scarcely influenced by polymerization solvents (Table I), but the values changed according to measurement solvents, and were in the range of -140.6° – -145.9° for poly(MBMOC), -87.3° – -101.7° for poly(MPMOC), -106.4° – -123.7° for poly(PhEMOC), and -42.0° – -56.5° for poly(PhPMOC), as shown in Figure 6A. Specific optical rotations of poly(RMOC)s measured at various temperatures in benzene are shown in Figure 6B. The absolute values of the specific optical rotations of poly(RMOC)s increased almost linearly with decrease in temperature, and these changes were reversible due in part to change in conformation caused by hydrogen bonds between urethane branches.

Figure 7 shows relationships between specific optical rotations and content (wt%) of monomeric unit of RMOC in poly(RMOC-co- M_2)s. Absolute specific optical rota-

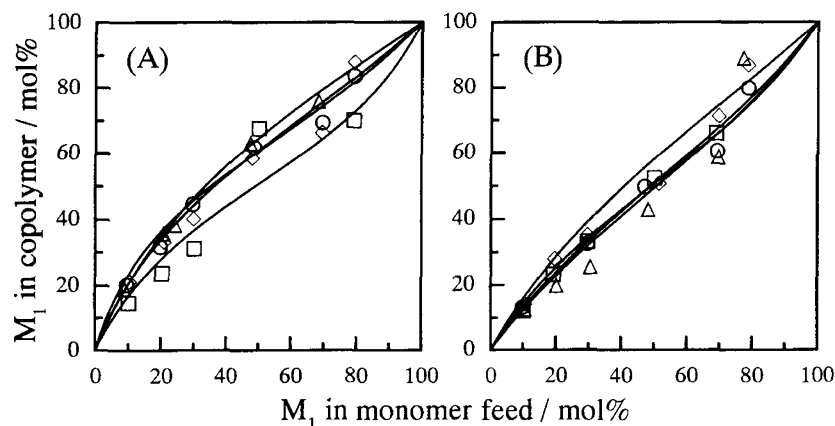


Figure 5. Copolymer composition curves for (A) RMOC-ST and (B) RMOC-MMA systems; RMOC=(○) MBMOC, (□) MPMOC, (△) PhEMOC, and (◇) PhPMOC.

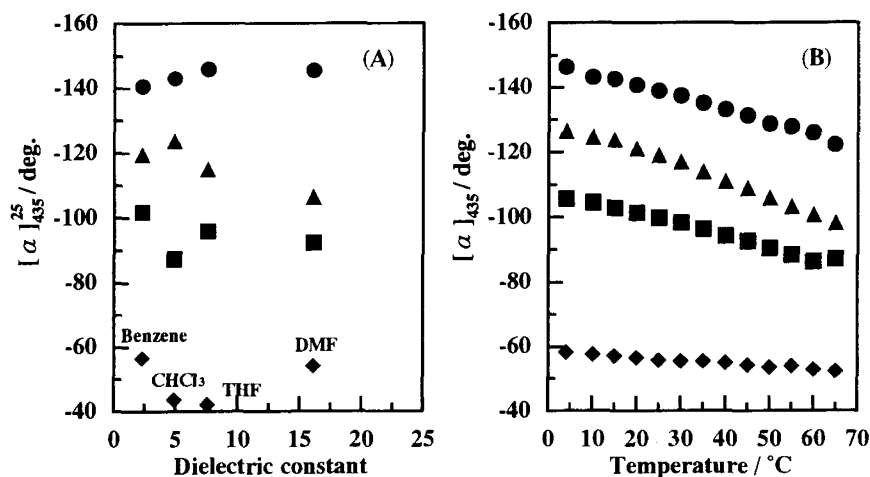


Figure 6. Relationships between specific optical rotations and (A) dielectric constants of solvents, and (B) measurement temperature in benzene: (●) poly(MBMOC), (■) poly(MPMOC), (▲) poly(PhEMOC), and (◆) poly(PhPMOC); $c = 1.0 \text{ g dL}^{-1}$, $l = 10 \text{ cm}$.

Table V. Radical copolymerizations of RMOC (M_1) with MOTSi (M_2) in THF (3 mL) at 60°C for 24 h^a and preparation of columns for HPLC

Run	Product	RMOC M_1	M_1 in monomer mol%	Yield ^b %	M_1 in copolymer ^c mol%	\bar{M}_n^d $\times 10^{-4}$	\bar{M}_w/\bar{M}_n^d	$[\alpha]_{435}^{25}$ ^e deg	Column ^f		
									Type of CSP	Content of poly (RMOC) _{segment} ^g wt%	Plate number ^h
1	MB 50	MBMOC	50.3	67.4	42.9	2.50	2.37	-95.5	type I	21	175
2	MB 100 ⁱ		100	66.5	100	0.38	1.43	ND	type II	30	494
3	MP 50	MPMOC	49.3	49.2	ND	1.52	3.47	-62.1 ^j	type I	24	483
4	MP 100 ⁱ		100	62.4	100	ND	ND	ND	type II	12	239
5	PhE 50	PhEMOC	49.3	78.6	42.7	2.36	2.47	-69.6	type I	31	191
6	PhE 100 ⁱ		100	72.1	100	ND	ND	ND	type II	31	264
7	PhP 50	PhPMOC	49.4	75.6	ND	1.42	3.03	-32.3 ^j	type I	25	342
8	PhP 100 ⁱ		100	69.8	100	0.18	1.91	ND	type II	34	327

ND, Not determined. ^a Initiator, 2,2'-azobisisobutyronitrile (AIBN) = 0.03 mol L^{-1} ; MOTSi, methacryloyloxypropyl trimethoxysilane; Run 1–3, 5, and 7–8: $M_1 + M_2 = 0.8 \text{ g}$; Run 4: $M_1 + M_2 = 2.0 \text{ g}$; Run 6: $M_1 + M_2 = 1.8 \text{ g}$. ^b MeOH-insoluble part. ^c By ¹H NMR. ^d By GPC with polystyrene standard. ^e $c = 1.0 \text{ g dL}^{-1}$, $l = 10 \text{ cm}$, THF. ^f Column, $150 \times 2 \text{ mm}$, in methanol. ^g By IR. ^h For toluene using methanol as eluent at flow rate 0.5 mL min^{-1} at ambient temperature. ⁱ Chain transfer agent, 3-mercaptopropyl trimethoxysilane = 0.06 mol L^{-1} . ^j $c = 1.0 \text{ g dL}^{-1}$, $l = 5 \text{ cm}$, THF.

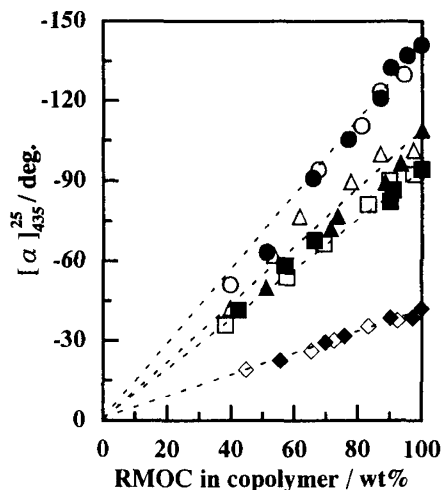


Figure 7. Relationships between specific optical rotations $[\alpha]_{435}^{25}$ and contents (wt%) of the monomeric unit of RMOC in copolymer; (●) poly(MBMOC-*co*-ST)s, (○) poly(MBMOC-*co*-MMA)s, (■) poly(MPMOC-*co*-ST)s, (□) poly(MPMOC-*co*-MMA)s, (▲) poly(PhEMOC-*co*-ST)s, (△) poly(PhEMOC-*co*-MMA)s, (◆) poly(PhPMOC-*co*-ST)s, and (◇) poly(PhPMOC-*co*-MMA)s.

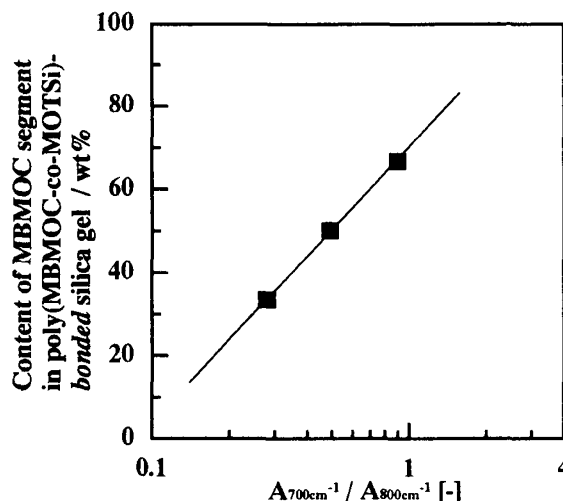


Figure 9. Calibration curve for content (wt%) of MBMOC segment in poly(MBMOC-*co*-MOTSi)-bonded silica gel.

seem scarcely influenced by *co*-units of ST or MMA.

Preparation of CSPs and Chiral Recognition Ability of poly(RMOC)s

To investigate chiral recognition ability of poly(RMOC), two of CSPs, poly(RMOC)-bonded silica gel (CSP-R100) and poly(RMOC-*co*-MOTSi)-bonded silica gel (CSP-R50), were prepared by the synthetic routes shown in Scheme 2. The reaction conditions and results are summarized in Table V. Figure 8 depicts IR spectra of poly(MBMOC), silica gel and poly(MBMOC-*co*-MOTSi)-bonded silica gel. For poly(MBMOC-*co*-MOTSi)-bonded silica gel, absorption due to phenyl groups appeared clearly at 700 cm^{-1} . RMOC segment content on CSPs was found with calibration curves, as shown in Figure 9, that were obtained from the ratios ($A_{700\text{ cm}^{-1}} / A_{800\text{ cm}^{-1}}$) of absorbance at 700 cm^{-1} and 800 cm^{-1} in IR spectra of suitable mixture of silica gel and chiral polymers.

The ability of CSPs prepared with RMOC for chiral recognition of racemates 1–12 (Scheme 3) was examined using HPLC. CSPs did not resolve all racemates in the normal phase such as 2-propanol/*n*-hexane, but resolved racemates 1–5 in the reversed phase such as methanol/ H_2O . Table VI shows the results of HPLC analysis using methanol/ H_2O as the mobile phase. Typical HPLC chromatograms of racemic manderic acid ethyl ester (1) in methanol/water = 7/3 with CSP-PhP100 are shown in Figure 10. Difference in chiral discriminating ability between CSPs of types I and II were observed. For example, ketoprofen (4) was not resolved on CSP-MP 50, but on CSP-MP 100. Thus, the chiral discriminating ability of poly(RMOC) may be due to the secondary and/or higher-ordered structure of the polymer. For racemate 1, separation factors for CSP-MP100 (or 50) and CSP-PhP (or 50) were larger than those for CSP-MB 100 (or 50) and CSP-PhE100 (or 50). Thus, the methylene group at the β -position in the amino acid residue of the RMOCs may play an important role in chiral discrimination.

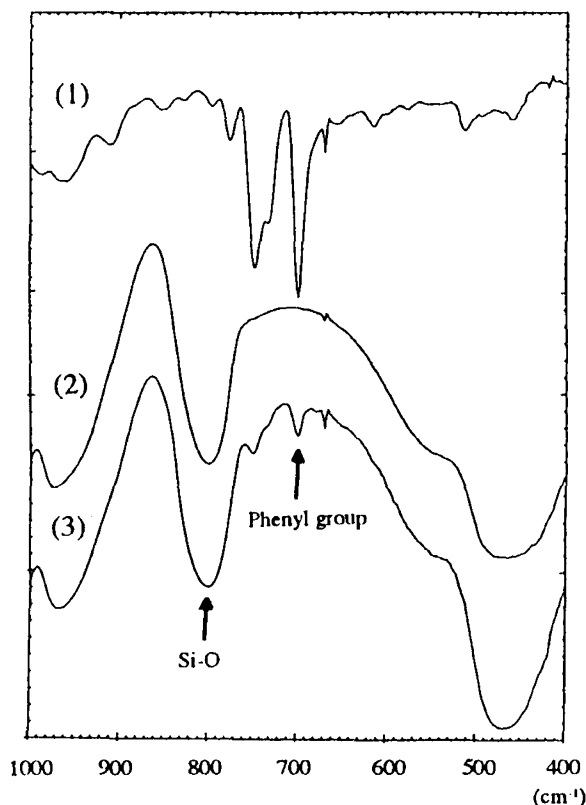
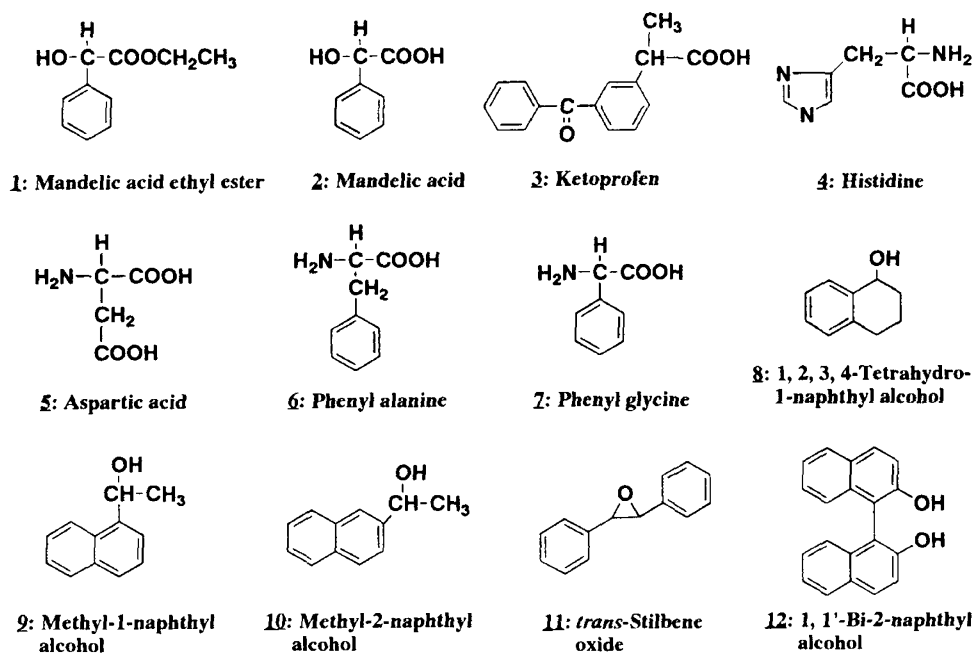


Figure 8. Infrared spectra for (1) poly(MBMOC), (2) silica gel, and (3) poly(MBMOC-*co*-MOTSi)-bonded silica gel.

tions of copolymers decreased with decreasing RMOC content, and the plots were extrapolated to 0° . The dotted lines refer to the relationship between specific optical rotation and content (wt%) of the RMOC unit in a mixture of a poly(RMOC) and poly(ST) or poly(MMA). Accordingly, the chiroptical properties of the copolymers



Scheme 3.

Table VI. Chromatographic resolution of racemates 1–12 on the CSP-R 100 (type I) and CSP-R 50 (type II)^a

Racemate	CSP-R 100 (type I)								CSP-R 50 (type II)							
	MB 100		MP 100		PhE 100		PhP 100		MB 50		MP 50		PhE 50		PhP 50	
	t_1^b	α^c	t_1	α	t_1	α	t_1	α	t_1	α	t_1	α	t_1	α	t_1	α
1	2.30	1.16	2.10	1.33	2.30	1.10	2.31	1.28	2.28	1.14	2.36	1.31	2.16	1.21	2.35	1.29
2	2.46 ^d	1.21	3.38	1.23	1.78 ^e	1.68	3.60 ^d	1.29	3.08	1.0	3.04 ^d	1.37	1.60 ^f	1.0	1.76	1.34
3	5.00	1.0	4.62	1.18	1.92	1.0	7.72	1.0	ND		7.72	1.0	1.56 ^f	1.0	2.28	1.0
4	3.50	1.0	3.92	1.0	1.48	1.0	4.00	1.0	3.34	1.0	1.96	1.34	3.58	1.0	2.04	1.27
5	2.24 ^d	1.47	5.00	1.0	2.04	1.0	ND		2.56	1.0	2.10	1.0	1.84 ^g	1.18	ND	
6	2.24	1.0	2.10	1.0	2.40	1.0	2.10	1.0	2.04	1.0	1.96	1.0	2.04	1.0	1.94	1.0
7	2.20	1.0	2.08	1.0	2.30	1.0	2.04	1.0	2.10	1.0	1.84	1.0	1.90	1.0	1.84	1.0
8	2.40	1.0	2.16	1.0	2.44	1.0	2.26	1.0	2.32	1.0	ND		2.40	1.0	2.54	1.0
9	3.46	1.0	3.84	1.0	3.20	1.0	4.12	1.0	3.28	1.0	4.74	1.0	3.62	1.0	3.86	1.0
10	2.56	1.0	2.26	1.0	2.56	1.0	2.74	1.0	2.52	1.0	2.90	1.0	2.50	1.0	2.84	1.0
11	5.36	1.0	3.56	1.0	4.60	1.0	7.40	1.0	4.80	1.0	8.56	1.0	6.16	1.0	6.02	1.0
12	4.72	1.0	3.06	1.0	4.90	1.0	5.10	1.0	3.50	1.0	5.50	1.0	3.40	1.0	4.80	1.0

ND, Not determined. ^a Eluent: MeOH/H₂O=7/3, flow rate=0.2 mL min⁻¹. ^b Retention time of the first-eluted enantiomer (min). ^c Separation factor= t_2 (retention time of the second-eluted enantiomer (min))/ t_1 . ^d Eluent: MeOH/H₂O=7/3. ^e Eluent: MeOH/H₂O=0/10. ^f Flow rate=0.05 mL min⁻¹. ^g Eluent: MeOH/H₂O=9/1.

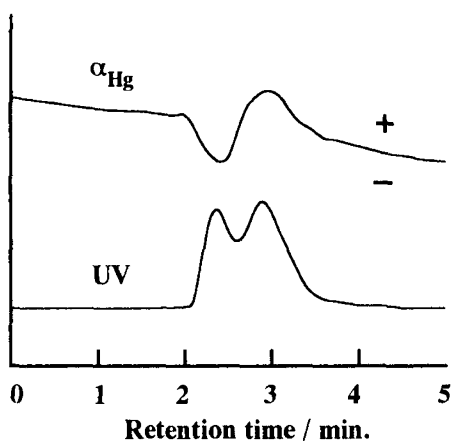


Figure 10. HPLC chromatograms of racemic mandelic acid ethyl ester (**1**) in a MeOH / H₂O (7 / 3) mobile phase; packing material, poly(PhMOC)-bonded silica gel (type I); column, 150 mm × 2 mm; flow=0.2 mL min⁻¹. Top and bottom curves were monitored by a UV (254 nm) and polarimetric detector, respectively.

CONCLUSION

Four new chiral methacrylates, MBMOC, MPMOC, PhEMOC, and PhPMOC, were synthesized from α -amino acids and MOI. Radical homopolymerizations of RMOC's were carried out in various solvents to obtain the corresponding polymers having hydrogen bonds due to urethane moieties. Chiroptical properties of poly-(RMOC)s were slightly influenced by dissolving solvents and temperature. Monomer reactivity ratios, Q , and e of RMOC were determined. Chiroptical properties of the copolymers were scarcely affected by co -units of ST and MMA. CSPs chemically prepared from RMOC's and silica gel proved for the resolution of racemic compounds **1–5** by HPLC.

REFERENCES

1. S. Matsuihiro, *Konbatekku*, **5**, 8 (1997).
2. a) H. Kamogawa, H. Kohno, and R. Kitagawa, *J. Polym. Sci., Part A: Polym. Chem.*, **27**, 487 (1989); b) C. Decker and K. Moussa, *Eur. Polym. J.*, **27**, 881 (1991); c) I. Francis, S. Arjen, C. Israel, and S. Johannes, *J. Polym. Sci., Part A: Polym. Chem.*, **31**, 239 (1993).
3. a) H. Albrecht and W. Wunderlich, *Angew. Makromol. Chem.*, **145/146**, 89 (1986); b) S. Savaskan and B. Hazer, *Angew. Makromol. Chem.*, **239**, 13 (1996); c) N. Monzner, U. K. Fischer, T. Volkel, and V. Rheinberger, *Angew. Makromol. Chem.*, **245**, 155 (1997).
4. C. H. Bamford, K. G. Al-Lamee, I. P. Middleton, J. Paprotny, and R. Carr, *Bull. Soc. Chim. Belg.*, **99**, 919 (1990).
5. Y. K. Lee, K. Onimura, H. Tsutsumi, and T. Oishi, *J. Polym. Sci., Part A: Polym. Chem.*, **38**, 4315 (2000).
6. S. G. Allenmark, "Chromatographic Enantioseparation", Ellis Howood Ltd., Chichester (1988).
7. For example, Y. Okamoto, *Chemtech*, **1987**, 176.
8. Y. Tamai, P. Qian, K. Matsunaga, and S. Miyano, *Bull. Chem. Soc. Jpn.*, **65**, 817 (1992).
9. a) G. Blaschke, *Angew. Chem., Int. Ed., Engl.*, **19**, 13 (1980); b) G. Blaschke, W. Broker, and E. Frankel, *Angew. Chem., Int. Ed., Engl.*, **25**, 830 (1986).
10. D. Arlt, B. Bomer, R. Grosser, and W. Lange, *Angew. Chem., Int. Ed., Engl.*, **30**, 1662 (1991).
11. T. Otsu and M. Kinoshita, "Koubunshigousei Jikkenhou" Kagakudoujin, Kyoto, Japan, 1972, pp 69–91.
12. A. Abiko and S. Masamune, *Tetrahedron Lett.*, **38**, 5517 (1992).
13. P. O'Brien, H. R. Powell, P. R. Raithby, and S. Warren, *J. Chem. Soc., Perkin Trans.*, **1**, 1031 (1997).
14. F. Tüdös, T. Kelen, T. Foldes-Berezsnich, and B. Turcsanyi, *J. Macromol. Sci., Chem.*, **A10**, 1513 (1976). The monomer reactivity ratios were determined by the method 6 described in this paper.
15. T. Jr. Alfrey and C. C. Price, *J. Polym. Sci.*, **2**, 101 (1947).