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Synthesis of novel chiral poly(methacrylate)s bearing urethane and cinchona alkaloid moieties in side chain and their chiral recognition abilities

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Abstract

Two types of new chiral methacrylates, cinchoninyl(2-methacryloyloxyethyl)carbamate (CIMOC) and cinchonidinyl(2-methacryloyloxyethyl)carbamate (CDMOC) were synthesized from 2-methacryloyloxyethyl isocyanate (MOI) and cinchona alkaloid such as cinchonine and cinchonidine, respectively. Radical polymerizations of CIMOC and CDMOC were performed under several conditions to obtain the corresponding polymers whose specific optical rotations ($[\alpha]_{435}^{25}$) were 84.0–89.0° and 0.39–0.72°, respectively. From the results of radical copolymerizations of RMOC (CIMOC and CDMOC, M_1) with styrene (ST, M_2) or methyl methacrylate (MMA, M_2), monomer reactivity ratios (r_1, r_2) and Alfrey–Price Q–e were determined: $r_1 = 0.18$, $r_2 = 0.48$, $Q_1 = 0.53$, $e_1 = 0.92$ for the CIMOC–ST system; $r_1 = 0.53$, $r_2 = 0.26$, $Q_1 = 4.91$, $e_1 = 1.80$ for the CIMOC–MMA system $r_1 = 0.59$, $r_2 = 0.47$, $Q_1 = 0.86$, $e_1 = 0.33$ for the CDMOC–ST system; $r_1 = 0.28$, $r_2 = 0.59$, $Q_1 = 2.15$, $e_1 = 1.74$ for the CDMOC–MMA system. The chiroptical properties of the copolymers were strongly influenced by *co*-units. Poly(RMOC)-bonded-silica gel as chiral stationary phase (CSP) was prepared for high performance liquid chromatography (HPLC). The CSPs resolved some racemates such as mandelic acid and *trans*-2-dibenzyl-4,5-di(*o*-hydroxyphenyl)-1,3-dioxolane by HPLC. The chiral recognition ability of poly(RMOC) may be due to the interaction between some cinchona alkaloid units and the racemates and/or to secondary and higher-ordered structures of the polymer. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: 2-Methacryloyloxyethyl isocyanate; Radical polymerization; Optical resolution

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1. Introduction

2-Methacryloyloxyethyl isocyanate (MOI) is a bifunctional monomer with both a reactive isocyanate group and a polymerizable double bond, and is convenient and widely used for crosslinking agents and materials for molecular design of new polymers [1]. Many kinds of MOI derivatives have been synthesized from several alcohols and amino compounds and polymerized [2–4]. However, there have been few reports on synthesis of MOI derivatives bearing an optically active group [5,6]. To our knowledge, no chiroptical properties of MOI derivatives with optically active groups have been reported. We lately reported on synthesis and polymerizations of some chiral methacrylate from MOI and chiral alcohols or amines such as cholesterol, L-menthol, amino acid derivatives, 2-hydroxy-2′-methoxy-1,1′-binaphthalene, (S)-methylbenzylamine, and L-phenylalanine methyl ester, and chiroptical properties of the polymers [7–9]. MOI is also useful for preparation of macro monomer [11–13]. We synthesized and polymerized N-substituted maleimide (RMI) macromonomers and examined from the view point of thermal stability of the polymers obtained [14]. Optically active acrylamide macromonomers were also synthesized and polymerized, and applied to chiral stationary phase (CSP) for high performance liquid chromatography (HPLC) [15].

Recently, a wide variety of CSPs have been developed for the separation of enantiomers by HPLC [16]. Although many kinds of synthetic chiral polymers have been applied to the CSPs, there have been few reports on preparation of CSPs for HPLC from poly(methacrylate)s bearing a chiral pendant group [17]. The reason may be that low chiral

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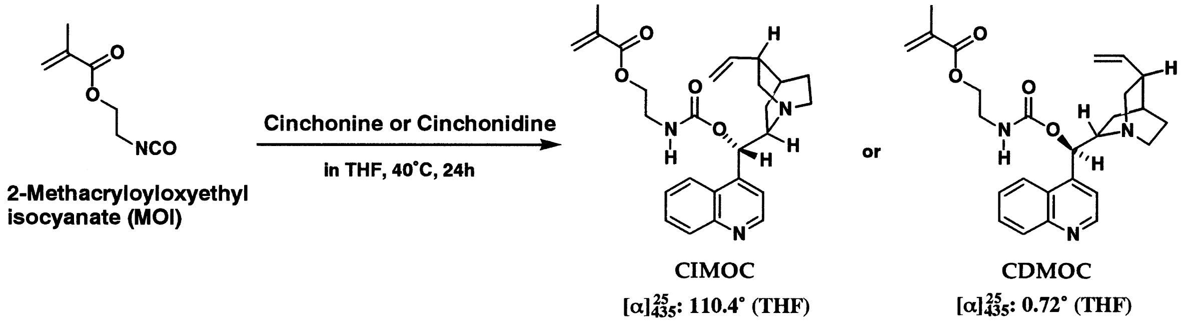


Scheme 1.

recognition ability of the chiral pendant group used and/or the absence of stable higher-ordered structures of the polymers [17]. Miyano et al. [18] synthesized optically active poly(methacrylate)s bearing a 1,1′-binaphthalene moiety as pendant group, and investigated on optical resolution ability as a chiral adsorbent for HPLC. However, the chiral recognition ability of the polymers was not based on higher-ordered structures of the polymer, but mainly interaction between the individual 1,1′-binaphthalene units and the racemates. Liu and Tsai [19] reported on optical resolution of racemates by chiral poly(methacrylate) having (+)-5-oxobornyl moieties. It is well known that poly(methacrylamide)s bearing a chiral pendant group are served as CSPs with outstanding recognition ability due to conformation controlled by hydrogen bonds between amide groups. Blaschke et al. [20,21] and Arlt et al. [22] reported the synthesis of many chiral poly(methacrylamide)s from α-amino acids or chiral amines and their chiral recognition abilities. We reported previously on preparations of new CSPs with chiral poly(methacrylate)s having urethane or urea bonds in the side chain and their chiral recognition abilities by HPLC [8–10].

This article describes the syntheses and polymerizations of two new chiral methacryloyloxyethyl carbamate (RMOC) from MOI and cinchona alkaloid such as cinchonine and cinchonidine, and application to CSP for HPLC. Radical homopolymerizability of RMOC, copolymerizability of RMOC with styrene (ST) or methyl methacrylate (MMA), and chiroptical properties of the polymers obtained are discussed. CSPs for HPLC are prepared from silica gel and the chiral poly(RMOC), and their optical resolution abilities are also investigated.

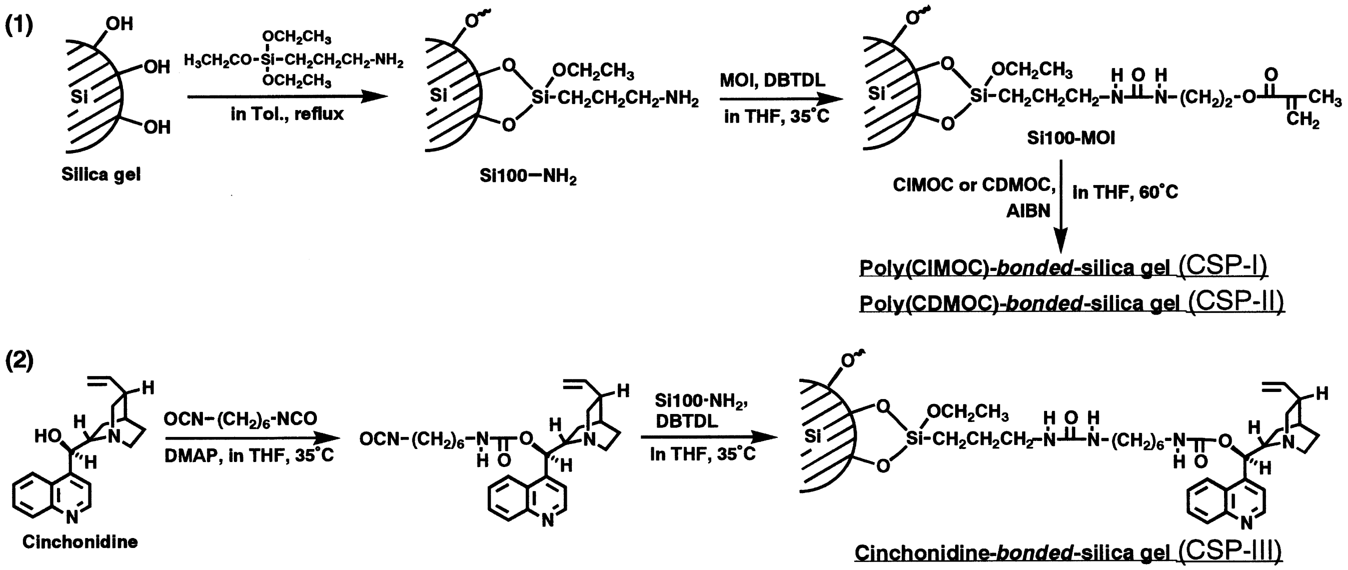
2. Experimental

2.1. Materials

Styrene (ST) and methyl methacrylate (MMA) were purified by the ordinary methods [23]. Tetrahydrofuran (THF), benzene, and toluene were dried over sodium metal and then used after distillation. *N*,*N*-Dimethylformamide (DMF), dichloromethane (CH_2Cl_2), chloroform ($CHCl_3$), acrylonitrile (CH_3CN) were used after distillation. 2,2′-Azobisisobutyronitrile (AIBN) was purified by recrystallization from methanol. Other reagents were used without further purification. Monomers of CIMOC and CDMOC were synthesized, as drawn in Scheme 1.

Cinchoninyl(2-methacryloyloxyethyl)carbamate (CIMOC). MOI (4.5 g, 2.7×10^{-2} mol) was added dropwise to a stirred solution of cinchonine (7.8 g, 2.7×10^{-2} mol) in THF (80 ml) under nitrogen at room temperature. The solution was heated at 40 °C and stirred for 24 h under nitrogen. The reaction mixture was evaporated under reduced pressure to give the crude product. Purification by recrystallization from ethyl acetate/*n*-hexane (1/1) gave CIMOC as white powder: yield 74.7%; mp 113–115 °C; $[\alpha]^{25}_{435}$ +110.4° ($c = 1.0$ g dl^{-1}, $l = 10$ cm, THF); ^{1}H-NMR (δ, ppm from TMS in $CDCl_3$) 8.88–7.36 (m, 6H, in quinoline group), 6.50–6.44 (d, 1H, $J = 7.58$, O–C*H), 6.08–5.99 (m, 2H, (*trans*) CH_2 = C(CH_3) and CH_2=C*H*), 5.52 (s, 1H, (*cis*) C*H*$_2$=C(CH_3)), 5.19–5.06 (m, 2H, N–H and C*H*$_2$=CH), 4.22–4.18 (m, 2H, $COOCH_2$), 3.48–3.44 (m, 2H, C*H*$_2$NH), 3.32–3.22 (m, 1H, N–C*H*$_2$–CH_2 (*exo*)), 3.00–2.86 (m, 2H, N–C*H*$_2$–CH (*exo*) and N–C*H*–CH_2), 2.76–2.65 (m, 2H, N–C*H*$_2$–CH_2 (*endo*) and N–C*H*$_2$–CH (*endo*)), 2.30–2.24 (m, 1H, CH_2=CH–C*H*), 1.87–1.73 (m, 6H, CH_2=C(C*H*$_3$), CH_2–C*H*–CH_2, N–CH_2–C*H*$_2$ (*exo*), and N–CH–C*H*$_2$ (*exo*)), 1.56–1.51 (m, 2H, N–CH_2–C*H*$_2$ (*endo*) and N–CH–C*H*$_2$ (*endo*)); ^{13}C-NMR (δ, ppm from TMS in $CDCl_3$) 167.26 (C=O), 155.42 (NH–CO), 149.90, 148.48, 145.93, 130.30, 129.08, 126.72, 125.93, 123.41, 118.51 (in quinoline group), 140.56 (CH_2=*C*H), 135.74 (CH_2=*C*(CH_3)), 126.09 (*C*H_2=C(CH_3)), 114.70 (*C*H_2=CH), 74.11 (O–*C**H), 63.40 (O–*C*H_2), 59.66 (N–*C*H–CH_2), 49.71 (N–*C*H_2–CH), 48.97 (N–*C*H_2–CH_2), 40.33 (CH_2NH), 39.75 (N–CH_2–*C*H), 27.75 (CH_2–*C*H–CH_2), 26.42 (N–CH_2–*C*H_2), 23.90 (N–CH–*C*H_2), 18.21 (CH_3). Anal. Calcd for $C_{26}H_{31}N_3O_4$: C, 69.47; H, 6.95; N, 9.35; Found: C, 70.87; H, 6.90; N, 9.10.

Cinchonidyl(2-methacryloyloxyethyl)carbamate (CDMOC). CDMOC as white powder was synthesized from MOI and cinchonidine by the same procedure for the synthesis of CIMOC. Purification by recrystallization from ethyl acetate gave CDMOC as white powder: yield 55.3%; mp 143–144 °C; $[\alpha]^{25}_{435}$ +0.72° ($c = 1.0$ g dl^{-1}, $l = 10$ cm,



Scheme 2.

THF); ^{1}H-NMR (δ, ppm from TMS in $CDCl_3$) 8.89–7.39 (m, 6H, in quinoline group), 6.48–6.45 (d, 1H, $J = 7.58$, O–C*H), 6.04 (s, 1H, (*trans*) $C\mathit{H}_2{=}C(CH_3)$), 5.90–5.80 (m, 1H, $CH_2{=}C\mathit{H}$), 5.52 (s, 1H, (*cis*) $C\mathit{H}_2{=}C(CH_3)$), 5.11 (bs, 1H, N–H), 5.04–4.98 (m, 2H, $C\mathit{H}_2{=}CH$), 4.22–4.17 (m, 2H, $COOCH_2$), 3.48–3.44 (m, 2H, $C\mathit{H}_2NH$), 3.35–3.32 (m, 1H, N–$C\mathit{H}_2$–CH_2 (*exo*)), 3.06–2.97 (m, 2H, N–$C\mathit{H}_2$–CH (*exo*) and N–$C\mathit{H}$–CH_2), 2.60–2.52 (m, 2H, N–$C\mathit{H}_2$–CH_2 (*endo*) and N–$C\mathit{H}_2$–CH (*endo*)), 2.28–2.20 (m, 1H, $CH_2{=}CH{-}C\mathit{H}$), 1.88–1.85 (m, 4H, $CH_2{=}C(C\mathit{H}_3)$ and CH_2–$C\mathit{H}$–CH_2), 1.77–1.69 (m, 2H, N–CH_2–$C\mathit{H}_2$ (*exo*) and N–CH–$C\mathit{H}_2$ (*exo*)), 1.58–1.51 (m, 2H, N–CH_2–$C\mathit{H}_2$ (*endo*) and N–CH–$C\mathit{H}_2$ (*endo*)); ^{13}C–NMR (δ, ppm from TMS in $CDCl_3$) 167.37 (C=O), 157.90 (NH–CO), 149.83, 148.45, 145.79, 130.15, 129.09, 126.72, 125.82, 123.36, 118.65 (in quinoline group), 141.67 ($CH_2{=}\mathit{C}H$), 135.89 ($CH_2{=}\mathit{C}(CH_3)$), 126.02 ($\mathit{C}H_2{=}C(CH_3)$), 114.36 ($\mathit{C}H_2{=}CH$), 74.29 (O–C*H), 63.25 (O–$\mathit{C}H_2$), 59.70 (N–CH–CH_2), 56.46 (N–$\mathit{C}H_2$–CH), 42.23 (N–$\mathit{C}H_2$–CH_2), 40.27 (CH_2NH), 39.36 (N–CH_2–CH), 27.64 (CH_2–CH–CH_2), 27.44 (N–CH_2–$\mathit{C}H_2$), 24.46 (N–CH–$\mathit{C}H_2$), 18.30 (CH_3). Anal. Calcd for $C_{26}H_{31}N_3O_4$: C, 69.47; H, 6.95; N, 9.35; Found: C, 70.97; H, 7.00; N, 9.05.

2.2. Radical polymerization

Radical homopolymerizations and copolymerizations were performed with AIBN as initiator in suitable solvent in a sealed tube at 60 °C. After polymerization the polymer solution was poured into a large amount of *n*-hexane or methanol/water (1/1) to precipitate the polymer. The obtained polymer was purified by reprecipitating it twice from the THF or DMF solution to excess *n*-hexane or methanol/water (1/1). The polymers were decanted and dried in vacuum for 3 days. The composition of the copolymer was calculated elemental analysis (N).

2.3. Preparation of CSPs for HPLC and column packing

Macroporous silica gel (TOSOH, TSK-GEL SI 100: mean particle size, 5 μm; pore size 100 Å), was silanized with 3-aminopropyl triethoxysilane according to the literature method [24]. MOI (16 ml) was added to a slurry of the silanized silica gel (8.0 g) under nitrogen. The mixture was heated at 35 °C, stirred for 45 h under nitrogen and then cooled to room temperature. The reaction mixture was filtered, washed with dichloromethane, acetone, and methanol, and then dried in vacuo to obtain silica gel containing vinyl groups on the surface (Si100–MOI in Scheme 2). Si100–MOI (1.0 g) and monomer (ClMOC or CDMOC (0.5 g) were weighed in a Shlenk's reaction tube. A solution of AIBN (3 mol% against monomer) in THF (10 ml) was added to the mixture in a Shlenk's reaction tube under nitrogen. The slurry was shaken at 60 °C for 48 h and cooled to room temperature. The reaction mixture was filtered, washed with DMF, THF, acetone, and methanol, and then dried in vacuo to afford CSP-I (monomer = ClMOC) and CSP-II (monomer = CDMOC).

To a mixture solution of cinchonidine (0.3 g, 1.0×10^{-3} mol) and DMAP (0.01 g, 8.2×10^{-5} mol) in THF (10 ml) was added hexamethylene diisocyanate (HDI, 0.19 ml, 1.2×10^{-3} mol) under nitrogen. The mixture was heated at 35 °C and stirred for 20 h under nitrogen. Si100–NH_2 (1.0 g) and di-*n*-butyltin dilaurate (DBTDL, 0.01 g, 1.6×10^{-5} mol) were added to the reaction mixture. The mixture was further stirred for 48 h at 35 °C under nitrogen, and then cooled to room temperature. The reaction mixture was filtered, washed with DMF, THF, acetone, and methanol, and then dried in vacuo to obtain cinchonidine-bonded-silica gel (CSP-III).

The contents (wt%) of polymer or cinchonidine segment on CSP-I–III were 24.3, 26.3, and 11.2 wt%, respectively, which were estimated from IR spectra, by

Table 1
Radical homopolymerizations of CIMOC and CDMOC for 24 h at 60 °C

Run	Monomer	Polym. solvent (ml)	Yield[a]	$\bar{M}_n$[b] ($\times 10^{-4}$)	$\bar{M}_w/\bar{M}_n$[b]	$[\alpha]^{25}_{435}$[c]
1	CIMOC	THF (2)	53.6	0.96	1.70	84.0
2	CIMOC	$CHCl_3$ (2)	69.1	1.60	2.18	89.0
3	CIMOC	Toluene (2)	87.4	–[d]	–[d]	–[d]
4	CIMOC	DMF (2)	68.0	–[d]	–[d]	–[d]
5	CDMOC	THF (4)	44.2	0.73	2.17	0.72
6	CDMOC	CH_2Cl_2 (2)	51.0	–[d]	–[d]	–[d]
7	CDMOC	Benzene (6)	Trace			
8	CDMOC	DMF (4)	61.1	2.14	1.45	0.39
9	CDMOC	CH_3CN (5)	Trace			

Monomer = 0.5 g, initiator; AIBN, $c = 0.03$ mol l^{-1}.

[a] Run 1–4: *n*-hexane insoluble part, run 5–9: H_2O/methanol = 1/1 insoluble part.

[b] By GPC with polystyrene standard.

[c] $c = 1.0$ g dl^{-1}, $l = 10$ cm, run 1–2 in THF; run 5, 8 in DMF.

[d] THF and DMF insoluble.

ordinary methods [8,9]. The CSPs were packed in a stainless steel HPLC column (i.d., 2 mm; length, 15 cm) by a slurry method. Theoretical plate numbers of the columns packed CSP-I–III were 1720, 1320, and 1400, respectively, which were measured for toluene in methanol or *n*-hexane/2-propanol (9/1) as eluent at a flow rate of 0.1 or 0.5 ml min^{-1} at 25 °C.

2.4. Measurements

NMR spectra were recorded at 25 °C using JEOL EX-270 (Jeol Ltd). Infrared spectra were recorded using Shimadzu FT IR-8100A (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 DMF as an eluent on a Shimadzu SPD-10A (Shimadzu Ltd) equipped with a UV detector, HSG-60 columns, and a 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, $c = 1.0$ g dl^{-1} in DMF). HPLC measurements were carried out on a Shimadzu LC-10AT (Shimadzu Ltd) equipped with UV detection at 254 nm.

3. Results and discussion

3.1. Radical homopolymerizations of CIMOC and CDMOC

Radical homopolymerizations of CIMOC and CDMOC were performed with AIBN as an initiator at 60 °C in various solvents, as summarized in Table 1. The polymerizations proceeded homogeneously expect for run 3, 4, and 6 in Table 1. All obtained polymers were white powders, though sticky and rubbery in methanol and *n*-hexane. For runs 3, 4, and 6 in Table 1, the polymers were insoluble in normal organic solvents such as acetone, THF, chloroform, and DMF, etc. It is difficult to clearly explain the reason, but the insoluble polymers may have high molecular weights or cross-linking structures. Fig. 1 shows ^{1}H-NMR spectra of CIMOC and poly(CIMOC). The peaks at 6.08 and 5.52 ppm assigned to vinyl groups (CH_2=C(CH_3)–)

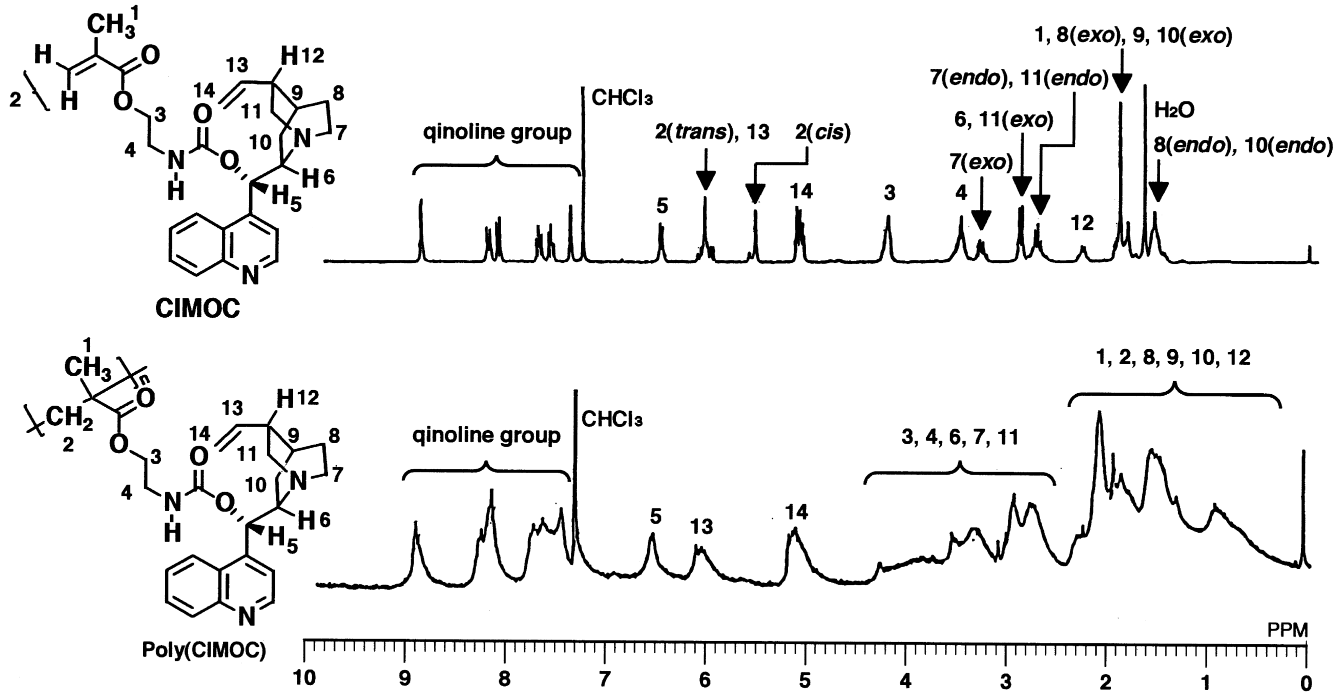


Fig. 1. ^{1}H-NMR spectra for CIMOC and poly(CIMOC) in $CDCl_3$ at 23.5 °C (270 MHz).

Table 2
Copolymerizations of CIMOC (M_1) and CDMOC (M_1) with ST(M_2) or MMA(M_2) in THF or DMF at 60 °C

Run	M_1	M_2	M_1 in monomer (mol%)	Polym. time (h)	Yield[a] (%)	M_1 in copolymer[b]		$\bar{M}_n$[c] ($\times 10^{-4}$)	$\bar{M}_w/\bar{M}_n$[c]	$[\alpha]_{435}^{25}$[d] (deg.)
						mol%	wt%			
1	CIMOC	ST	20.2	9.0	34.1	26.1	60.4	1.18	3.22	54.4
2	CIMOC	ST	40.3	7.0	43.5	30.4	65.4	1.06	1.99	87.2
3	CIMOC	ST	59.2	3.5	52.7	57.4	85.3	2.46	4.20	87.3
4	CIMOC	ST	79.1	4.0	23.3	58.7	86.0	0.52	1.73	88.2
5	CIMOC	MMA	19.9	2.0	36.5	32.3	68.2	3.65	5.90	62.5
6	CIMOC	MMA	38.8	2.0	45.4	49.0	81.2	–[e]	–[e]	–[e, f]
7	CIMOC	MMA	58.5	2.0	39.8	55.4	84.8	–[e]	–[e]	–[e, f]
8	CIMOC	MMA	79.8	2.0	34.6	77.4	93.9	–[e]	–[e]	–[e, f]
9	CDMOC	ST	19.4	12	15.9	25.0	59.0	1.41	3.21	15.7
10	CDMOC	ST	40.1	12	25.6	38.6	73.1	1.34	2.20	18.8
11	CDMOC	ST	59.8	12	27.1	40.6	74.7	4.20	1.08	18.4
12	CDMOC	ST	78.4	12	31.6	86.4	96.5	1.49	3.19	15.3
13	CDMOC	MMA	10.0	3.8	6.3	12.5	39.0	–[e]	–[e]	7.9
14	CDMOC	MMA	20.0	1.7	16.8	25.5	60.5	–[e]	–[e]	14.0
15	CDMOC	MMA	30.0	2.0	10.6	30.0	65.7	–[e]	–[e]	17.1
16	CDMOC	MMA	48.0	2.4	8.3	46.3	79.5	–[e]	–[e]	17.3
17	CDMOC	MMA	70.0	3.8	40.0	64.4	89.0	–[e]	–[e]	18.8
18	CDMOC	MMA	82.0	3.8	22.8	63.1	88.5	–[e]	–[e]	17.5

$M_1 + M_2 = 0.5$ g; initiator: 2,2′-azobisisobutyronitrile = 0.03 mol l^{-1}; run 1–8 in THF (1 ml); run 9, 13 in DMF (1 ml); run 10–12, 14 in DMF (2 ml); run 15 in DMF (3 ml); run 16–18 in DMF (4 ml).

[a] Run 1–8: *n*-Hexane-insoluble part; run 9–18: H_2O/methanol = 1/1 insoluble part.

[b] By elemental analysis (N).

[c] By GPC with polystyrene standard.

[d] $l = 5$ cm, $c = 1.0$ g dl^{-1}, run 1–5: in THF; run 9–18: in DMF.

[e] THF insoluble.

[f] DMF insoluble.

disappeared after polymerization, indicating that the radical polymerization completely proceeded. Number average molecular weights (M_n) of poly(CIMOC) and poly(CDMOC) were 9600–16,000 and 7300–21,400, respectively. Specific optical rotations ($[\alpha]_{435}^{25}$) of poly(CIMOC) and poly(CDMOC) were 84.0–89.0° and 0.39–0.72° in THF, respectively.

3.2. Radical copolymerizations of CIMOC and CDMOC with ST or MMA

The results of radical copolymerizations of CIMOC (M_1) and CDMOC (M_1) with ST(M_2) or MMA(M_2) using AIBN in THF or DMF at 60 °C are summarized in Table 2. The copolymerizations proceeded homogeneously throughout

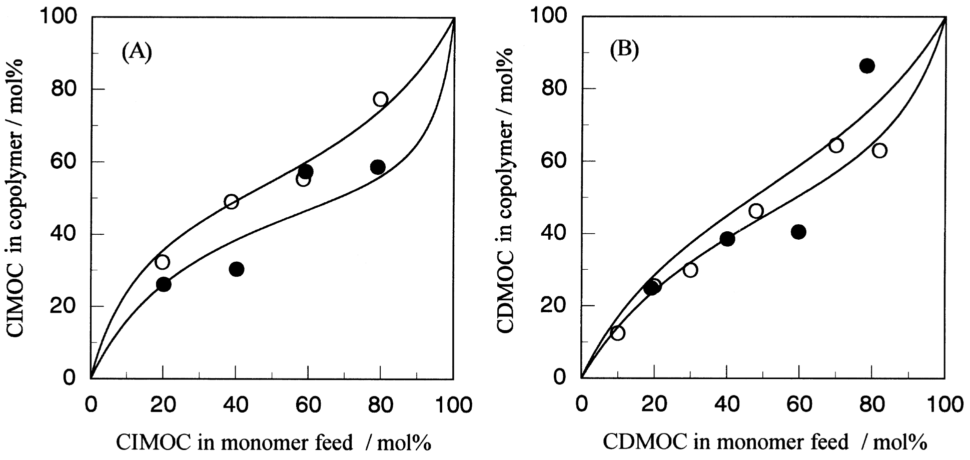


Fig. 2. Copolymer composition curves of (A) poly(CIMOC-*co*-M_2) and (B) poly(CDMOC-*co*-M_2); M_2 = (●) ST and (○) MMA.

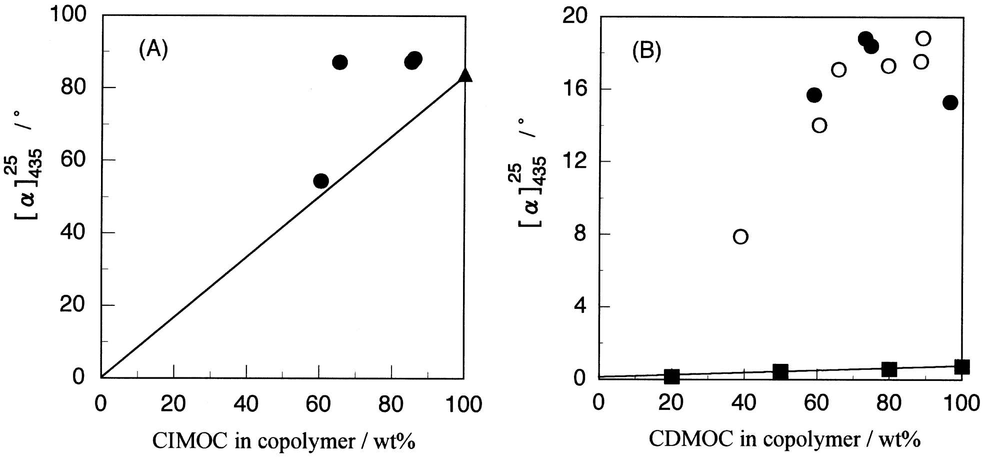


Fig. 3. Relationships between specific optical rotations ($[\alpha]^{25}_{435}$) and the content (wt%) of the monomeric unit of CIMOC and CDMOC in copolymer; (A) poly(CIMOC-*co*-M_2) and (B) poly(CDMOC-*co*-M_2); M_2 = (●) ST and (○) MMA; (▲) poly(CIMOC); (■) mixtures of poly(CDMOC) and poly(ST).

except for runs 6–8. Obtained copolymers were colorless powders.

Copolymer composition curves for the polymerizations of CIMOC and CDMOC with ST or MMA are shown in Fig. 2. Monomer reactivity ratios (r_1, r_2) calculated from the high-conversion method reported by Tüdös et al. [25] and Alfrey–Price Q–e values [26] for CIMOC and CDMOC were determined as follows: $r_1 = 0.18$, $r_2 = 0.48$, $Q_1 = 0.53$, $e_1 = 0.92$ in the CIMOC–ST system; $r_1 = 0.53$, $r_2 = 0.26$, $Q_1 = 4.91$, $e_1 = 1.80$ in the CIMOC–MMA system; $r_1 = 0.59$, $r_2 = 0.47$, $Q_1 = 0.86$, $e_1 = 0.33$ in the CDMOC–ST system; and $r_1 = 0.28$, $r_2 = 0.59$, $Q_1 = 2.15$, $e_1 = 1.74$ in the CDMOC–MMA system. Q_1 and e_1 values in the M_1–ST system were apparently different from those in the M_1–MMA system. The reason may result from no consideration of steric effect in the Alfrey–Price Q and e theory. It seems that CIMOC and CDMOC have relatively high steric hindrance because of a large substituent group such as cinchona alkaloid.

Fig. 3 shows relationships between specific optical rotation and content (wt%) of the monomeric unit of RMOC (CIMOC and CDMOC) in poly(RMOC-*co*-M_2)s. A line connecting 0° with $[\alpha]^{25}_{435}$ of poly(RMOC) refers to relationships between the specific optical rotation and the contents (wt%) of monomeric unit in a mixture of poly(RMOC) and poly(ST) [or poly(MMA)]. In Fig. 3, the specific optical rotations of poly(CIMOC-*co*-ST)s and poly(CDMOC-*co*-M_2)s showed a large deviation from the line, suggesting that chiroptical property of the copolymers depend strongly on *co*-units (ST or MMA monomeric unit).

Fig. 4 shows dependence of specific optical rotations of poly(CDMOC-*co*-M_2)s on a diad sequence ($P_2[m_1m_2]$) [27, 28] and average sequence length of CDMOC units (l_1) [29]. $P_2[m_1m_2]$ indicates probability of a M_1–M_2 diad sequence. $P_2[m_1m_2]$ was derived as follows:

$$P_1[m_1] + P_1[m_2] = 1$$

$$P_2[m_1m_2] = P_1[m_1]P(m_1m_2)$$

$$P(m_1m_2) = 1/(1 + r_1X)$$

where $P_1[m_1]$ and $P_1[m_2]$ are molar fractions of the copolymer, $P(m_1m_2)$ is given by the monomer molar ratio

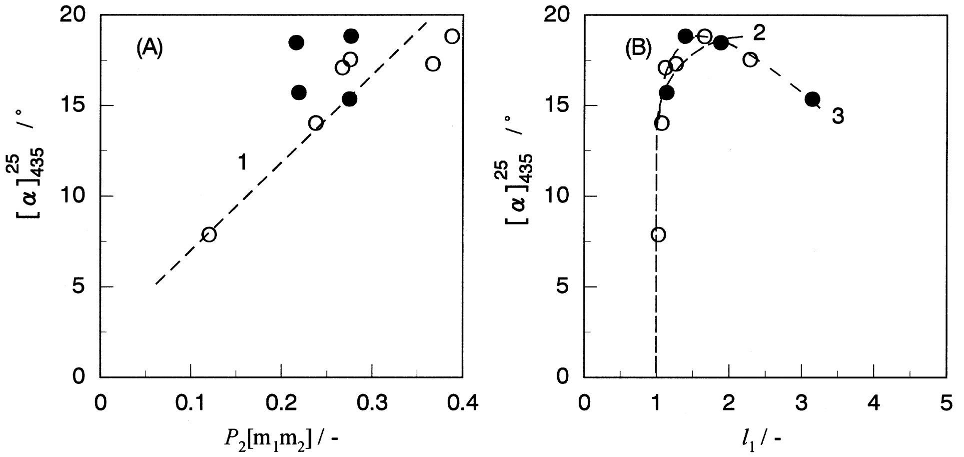
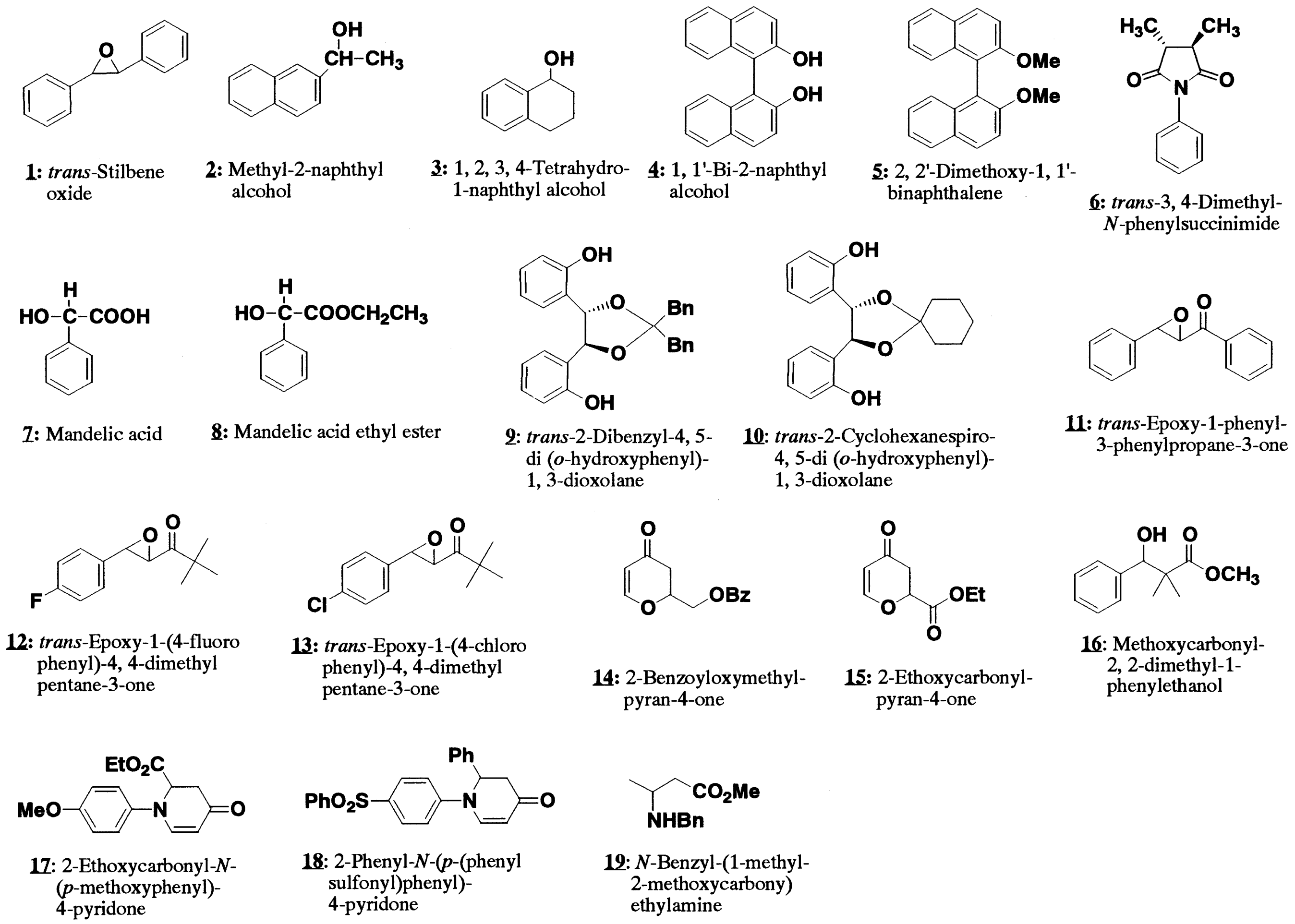


Fig. 4. Relationships between specific optical rotations ($[\alpha]^{25}_{435}$) of poly(CDMOC-*co*-M_2)s and (A) the diad sequence ($P_2[m_1m_2]$) and (B) the average sequence length (l_1); M_2 = (●) ST and (○) MMA.



Scheme 3.

in the feed ($X = M_1/M_2$), and r_1 in the monomer reactivity ratio of CDMOC. In CDMOC–MMA, specific optical rotations increased with increasing the diad sequence, and the relationships showed good linearity (broken line 1). And specific optical rotations increased with maintaining nearly 1.0 of average sequence length (broken line 2). These results indicate that chiroptical properties of the polymers were strongly influenced by the CDMOC–MMA sequence. On the other hand, such a linear relationship between specific optical rotation and diad sequence was not observed for the CDMOC–ST system, suggesting that chiroptical properties of the copolymers were influenced by both the CDMOC–ST diad sequence and the average sequence length of CDMOC units in poly(CDMOC-*co*-ST)s, as shown in Fig. 4(B), broken line 3.

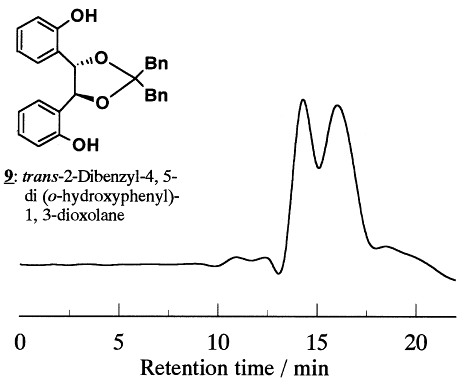


Fig. 5. Typical HPLC chromatogram of racemate *9* with CSP-I in *n*-hexane/2-propanol ($9.5/0.5_{\text{volume}}$) mobile phase; CSP-I: poly(CIMOC)-bonded-silica gel; racemate *9*: *trans*-2-dibenzyl-4, 5-di(*o*-hydroxyphenyl)-1,3-dioxolane; column size: 150 mm × 2 mm; flow = 0.05 ml min^{-1}.

3.3. Optical resolution ability of poly(CIMOC) and poly(CDMOC)

To investigate chiral recognition ability of poly(RMOU), two types of chiral stationary phases (CSPs), poly(CIMOC)-bonded-silica gel (CSP-I) and poly(CDMOC)-bonded-silica gel (CSP-II), were prepared according to synthetic routs of Scheme 2(1). Poly(RMOC) has urethane bonds and bulky quinoline moieties which can serve as π-electron donor group. Hence, hydrogen bond and π–π interaction are expected between the CSPs and racemates having a carbonyl, a hydroxyl, and an aromatic group. The abilities of the CSPs for chiral recognition of racemates **1–19** (Scheme 3) were examined with HPLC. The CSP-I and

Table 3
Chromatographic resolution of racemates **1-19** on CSP-I–III

Racemates	CSP-I				CSP-II				CSP-III			
	$k'1$[a]	$k'2$[a]	α[b]	Rs[c]	k'_1	k'_2	α	Rs	k'_1	k'_2	α	Rs
1	0.21	0.21	1.00		0.46	0.46	1.00		0.16	0.16	1.00	
2	1.17	1.17	1.00		1.07	1.07	1.00		0.94	0.94	1.00	
3	0.47	0.47	1.00		0.82	0.82	1.00		0.34	0.34	1.00	
4	4.64	4.64	1.00		7.97	7.97	1.00		3.55	3.55	1.00	
5	0.71	0.71	1.00		1.08	1.08	1.00		–[d]	–[d]	–[d]	
6	1.29	1.29	1.00		1.92	1.92	1.00		0.54	0.54	1.00	
7	1.39	1.39	1.00		0.57	1.06	1.88	1.02	0.73	0.73	1.00	
8	0.43	0.43	1.00		0.69	0.69	1.00		0.32	0.32	1.00	
9	2.30[e]	2.81	1.22	0.58	0.56	0.79	1.42	0.70	0.20	0.20	1.00	
10	2.81[e]	3.24	1.16	0.59	0.53	0.53	1.00		3.08	3.08	1.00	
11	1.58	1.58	1.00		1.75	1.75	1.00		0.68	0.68	1.00	
12	0.57	0.57	1.00		0.51	0.51	1.00		0.30	0.30	1.00	
13	1.51	1.51	1.00		0.72	0.72	1.00		0.73	0.73	1.00	
14	1.49	1.49	1.00		2.02	2.02	1.00		0.61	0.61	1.00	
15	1.82	1.82	1.00		2.66	2.66	1.00		0.75	0.75	1.00	
16	0.58	0.58	1.00		0.86	0.86	1.00		0.60	0.60	1.00	
17	–[d]	–[d]	–[d]		3.56	3.56	1.00		–[d]	–[d]	–[d]	
18	–[d]	–[d]	–[d]		2.30	2.30	1.00		1.48	1.48	1.00	
19	0.46	0.46	1.00		0.58	0.70	1.20	0.36	0.17	0.17	1.00	

CSP-I, poly(CIMOC)-bonded-silica gel; CSP-II, poly(CDMOC)-bonded-silica gel; CSP-III, cinchonidine-bonded-silica gel; mobile phase, *n*-hexane/2-propanol = $9/1_{\text{volume}}$; flow = 0.1 ml min^{-1}.

[a] Capacity factor of enantiomer eluting first (k'_1) and second (k'_2) = (retention time of enantiomer void time of column)/(retention time of 1,3,5-*t*-butylbenzene).

[b] Separation factor = k'_2/k'_1.

[c] Resolution factor = 2 × (distance between the peaks of more and ress retained enantiomers)/(sum of bandwidth of two peaks).

[d] Not determined.

[e] Mobile phase, *n*-hexane/2-propanol = $9.5/0.5_{\text{volume}}$; flow = 0.05 ml min^{-1}.

CSP-II resolved some racemates in normal phase such as *n*-hexane/2-propanol, but did not resolve all racemates in reversed phase such as methanol/water. The results of chromatographic resolution in *n*-hexane/2-propanol are summarized in Table 3. Namely, CSP-I resolved racemates **9** and **10** in Scheme 3 using 5% 2-propanol in *n*-hexane as eluent. Racemates **7**, **9**, and **19** in Scheme 3 were resolved on CSP-II using 10% 2-propanol in *n*-hexane as eluent. Typical chromatogram of the resolution of racemate **9** on CSP-I is shown in Fig. 5. To examine the difference of chiral recognition ability between the polymeric chiral selector and the corresponding low molecular weight chiral selector, cinchonidine-bonded-silica gel (CSP-III) was prepared by synthetic routs of Scheme 2(2). No CSP-III could resolve all racemates **1**–**19**. Thus, it seems that only one unit of cinchona alkaloid cannot have chiral recognition ability. That is, the chiral recognition ability of CSP-II may be based on the interaction between some cinchona alkaloid units and the racemates and/or on secondary and higher-ordered structures of the polymer.

4. Conclusion

1. Two types of new chiral methacrylates bearing an carbamate moiety, CIMOC and CDMOC, were synthesized from MOI and cinchonine or cinchonidine.
2. Radical homopolymerizations of CIMOC and CDMOC were carried out in various solvents to obtain the corresponding chiral polymers.
3. From the results of the copolymerizations of CIMOC and CDMOC with ST or MMA, monomer reactivity ratios, *Q*, and *e* values were determined. Chiroptical properties of the copolymers were significantly influenced by comonomer-units.
4. CSPs prepared from silica gel and poly(RMOC) resolved racemates **7**, **9**, **10**, and **19** by HPLC. The chiral recognition ability may be attributed to the interaction between some cinchona alkaloid units and the racemates and/or to secondary and higher-ordered structures of the polymer.

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