Synthesis of Chiral Polymers Containing the Acetoxybornyl Group and Their Applications on the Asymmetric Induction

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SYNOPSIS

Optically active 2-endo-actoxy-5-endo-bornyl methacrylate (ABMA) was prepared from (+)-camphor. The homopolymerization of ABMA and copolymerization of ABMA with achiral methyl methacrylate (MMA) or styrene (St) were carried out with 2,2'-azobisisobutyronitrile (AIBN) in benzene. Effects of temperature, solvents, and reaction time on the copolymerization were discussed. The monomer reactivity ratios (r_1, r_2) for poly(ABMA-co-MMA) and poly(ABMA-co-St) and Q and e values for the chiral ABMA in the copolymerization systems were evaluated by the Fineman–Ross method. The absolute value of the specific rotation of poly(ABMA-co-MMA) increased with increasing ABMA unit content. A small deviation from linearity was observed, which suggests that asymmetry is not introduced into the copolymer main chain. Temperature and solvent effects on the specific rotation of the chiral homopolymer and copolymers were investigated. The results suggest that the chiral polymers synthesized in this investigation did not show a strong preference for a particular helical conformation. Applications of the chiral polymers on the asymmetric addition of n-butyllithium to aldehydes were also discussed.

INTRODUCTION

A large number of studies have been done to produce optically active compounds by asymmetric induction.[1,2] Homogeneous low molecular weight models often have the advantages of giving high stereoselectivity. Also, every molecule of the chiral catalyst is available to the reactants. In most cases, however, the asymmetric source is expensive and the preparation of asymmetric catalysts is so troublesome that it becomes desirable to use the catalyst repeatedly. This leads to the preparation of polymeric chiral catalysts.

Many studies have been reported on the systhesis of chiral compounds containing bornane groups derived from (+)-camphor.[3–5] There have been a few investigations on the synthesis of chiral polymers containing bornane moieties,[6,7] especially of chiral monomers derived directly from (+)-camphor.

During the course of our investigations on the synthesis of both monomers and polymers containing the (+)-bornane group, it was found that polymers with pendant chiral bornyl groups are effective for asymmetric induction reactions.[8–11] In connection with the studies on the catalytic functionality of the polymers having bornyl groups, the synthesis and polymerization of a new chiral monomer, 2-endo-acetoxy-5-endo-bornylmethacrylate (ABMA) was studied.

In this paper, the optically active ABMA was prepared, homopolymerized, and copolymerized with methyl methacrylate (MMA) or styrene (St). The monomer reactivity ratios were calculated, and Q and e values for ABMA were also determined. Effects of temperature, solvents, and reaction time on the specific rotation of chiral polymers were discussed. Applications of the chiral polymers having acetoxybornyl groups on the asymmetric addition

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of n-butyllithium to aldehydes were also investigated.

EXPERIMENTAL

Measurements

IR were recorded on a Hitachi 260-30 grating IR spectrophotometer. NMR spectra were recorded on a Bruker-100 high-resolution spectrometer. Optical rotations were measured at 20°C using a Jasco DIP-360 automatic digital polarimeter with readings to ±0.001°. Elemental analyses were calculated with a Heraeus CHN—O-rapid elemental analyzer.

(+)-5-endo-Hydroxybornyl Acetate (3)

(+)-5-endo-Hydroxybornyl acetate ((3) was prepared by reduction of (+)-5-oxo-bornyl acetate (2) with sodium borohydride in dry solvent. The latter compound was obtained by oxidation of (+)-bornyl acetate as previously described.[12] To (+)-5-oxo-bornyl acetate (2) [27.3 g, from (+)-bornyl acetate (1)] in dry ether (30 mL) was added to sodium borohydride (5.2 g) slowly at room temperature and then stirred for 24 h. After the reaction, excess sodium borohydride that remained was decomposed by adding 2N HCl solution dropwise. The reaction mixture was extracted with ether and dried over anhydrous magnesium sulfate. Ether was then evaporated to afford the crude products, which was distilled in vacuo to give (+)-3 in high purity; bp 120°C/10 Torr in yield of 19.90 g (72.8%); $[\alpha]_D$ = +16.75 (2.0 cg/mL; $CHCl_3$); IR(neat): 3600 cm^{-1} (OH), and 1750 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$): δ = 0.96 (m; 9H, 3CH$_3$), 1.86(s; 3H, CH$_3$CO), 2.65(s; 1H, endo-OH), 5.17(d; 1H, 2-exo-H).

ANAL.: $C_{11}H_{20}O_3$(200). Calcd: C, 66.00%; H, 10.00%.

Found: C, 65.98%; H 10.03%.

(+)-2-endo-Acetoxy-5-endo-bornyl Methacrylate (4)

A mixture of (+)-(3) (18 g, 85 mmol), methacrylic acid (20 mL, 136 mmol), and p-toluenesulfonic acid (2 g) was heated in 100 mL of benzene at 100°C for 20 h, in the presence of hydroquinone (2.0 g). Water liberated during the reaction was removed by molecular sieves (0.3 nm, Merck Co.). After completion of the reaction, the resulting mixture was washed with dilute sodium hydrogen carbonate solution twice and then with water three times. The oily layer was separated, dried over anhydrous magnesium sulfate, and distilled in vacuo (110°C/5 Torr) to yield 10.4 g (43.7%) of product. $[\alpha]_D$ = +15.38 (2.0 cg/mL, $CHCl_3$); IR(neat): 1750 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$): δ = 0.95 (m; 9H, 3CH$_3$), 1.84(s; 3H, CH$_3$CO), 1.89(s; 3H, C=CCH$_3$), 5.17 (d; 1H, 2-exo-H), 6.1(each s; 1H, C=CH$_2$).

ANAL.: $C_{15}H_{24}O_4$(268). Calcd: C, 67.16%; H, 8.96%.

Found: C, 67.12%; H, 8.94%.

Polymerization of Monomers

Chiral monomer (+)-(4) (10 g, 37.3 mmol) was polymerized in the presence of 2,2'-azobisisobutyronitrile (AIBN) in benzene (10 mL) at 60°C for 20 h. After polymerization, polymers were precipitated from a large amount of methanol, and only a trace of chiral homopolymer was obtained: $[\alpha]_D$ = +13.20 (2.0 cg/mL, benzene). Copolymerization of ABMA with various comonomers of MMA, St, and acrylonitrile (AN) were carried out in benzene

Table I   Copolymerization of ABMA with Various Comonomers[a]

Entry	Feed ABMA (mol %)	Comonomer	Conversion (%)[b]	Content of ABMA[c]	$[\alpha]_D^{25}$ (c,g/mL)	MW[d] ($\times 10^{-4}$)
				Chiral Polymer		
1	100	—	Trace	100	+15.20 (0.05)	1.2
2	26.3	MMA	43.15	12.0	+1.78 (0.07)	8.7
3	27.1	St	23.37	24.1	+3.96 (0.13)	4.8
4	20.0	AN	26.52	9.6	+1.47 (0.12)	5.1

[a] At 60°C in benzene with 1 wt % AIBN for 10 h.
[b] (Weight of polymer/total weight of monomer) × 100.
[c] Evaluated by elemental analysis.
[d] Molecular weight, evaluated by GPC.

at 60°C for a certain polymerization time, and the results are shown in Table I. The monomer, solvent, and AIBN were charged in this order into a polymerization tube, which was degassed *in vacuo* by a freeze-thaw technique and then sealed off. After a certain polymerization time, the tube was opened and the mixture was poured into a large excess of methanol to precipitate the polymer. the crude polymer was purified by reprecipitation using the benzene/methanol system. The conversion was calculated by gravimetry, and the compositions of the chiral polymers were calculated from the values of the elemental analyses.

Asymmetric Additions

Reactions involving air-sensitive compounds were carried out under inert atmosphere. Butyllithium was added to a dry THF solution (50 mL) of linear chiral polymer (**7**) (1.5 mmol of chiral units) (1.2 mmol, 15 wt % in hexane) at 0°C under a nitrogen atmosphere. After stirring for 1 h, the reaction mixture was cooled (or heated) to a given temperature for 10 h with stirring, and the aldehyde (1 mmol in dry THF) was added to it, which was then stirred for an additional 10 h. The reaction mixture was treated with 2N HCl, and THF was distilled off. The aqueous layer that resulted was extracted several times with ether. The combined ether solution was washed with water and dried over anhydrous magnesium sulfate, and the organic phase was then concentrated. The resulting oily product was poured into a large excess of methanol to precipitate the chiral polymer. After the chiral polymer was filtered off, the clear solution was then concentrated. Pure

product was isolated using a silica gel column and purified, subsequently, by bulb-to-bulb distillation and identified by NMR and IR analyses. The optical purity was calculated using the measured optical rotation.

RESULTS AND DISCUSSION

Chiral monomer ABMA (**4**) was synthesized from bornyl acetate (**1**) as shown in Scheme 1. (+)-5-Oxobornyl acetate (**2**), obtained from (+)-bornyl acetate (**1**) by chromium trioxide oxidation, was reduced to (+)-5-*endo*-hydroxybornyl acetate (**3**), which was treated with methacrylic acid to yield the new chiral monomer (+)-2-*endo*-acetoxy-5-endo-bornyl methacrylate (ABMA) (**4**). Structures of the synthesized compounds shown in Scheme 1 were all confirmed by elemental analysis, ^{1}H-NMR, and IR spectroscopy. The ^{1}H-NMR signal of the hydroxy group in position 5 shifted from $\delta = 3.4$ to upfield $\delta = 2.65$, showing that the hydroxy group is linked at the *endo* position.[13] The free radical polymerization of the chiral monomer ABMA (**4**) was carried out at 60°C in benzene. It was found that a large steric hindrance existed between the chiral monomers and that only a trace of chiral homopolymers can be obtained. To relieve the steric hindrance and synthesize chiral polymers containing the chiral unit (**4**), copolymerization of ABMA with the achiral comonomers of MMA, St, and AN were carried out at 60°C in the presence of AIBN. The results are summerized in Table I. Copolymers so-synthesized were confirmed by NMR and IR spectroscopy, and the compositions of the chiral polymers were calculated from the values of elemental analyses.
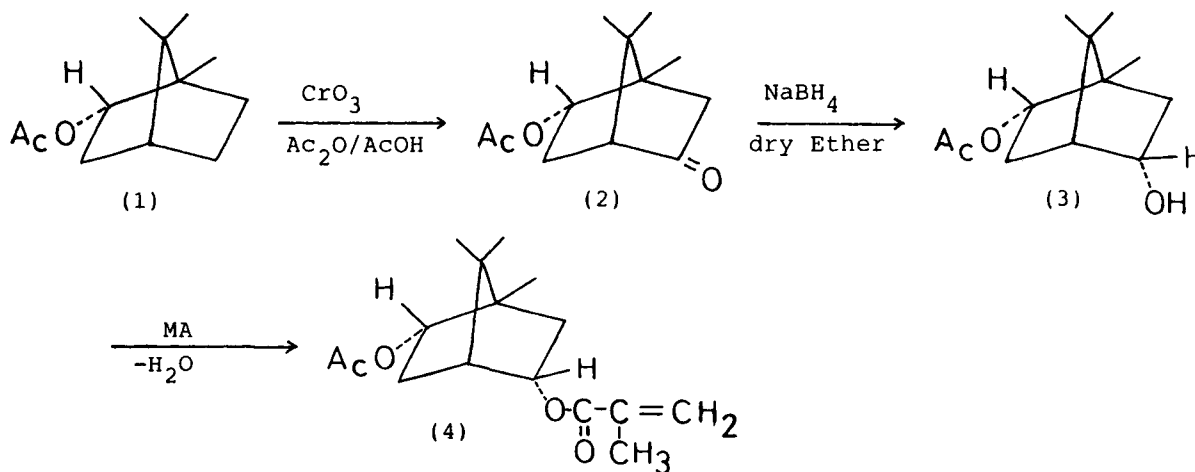
Scheme 1

As shown in Table I, conversions and the molecular weight of the copolymers (entries 2, 3, 4) are higher than those of the homopolymers (entry 1). This result suggests that a suitable low steric hindrance comonomer might be used as a spacer to decrease the steric hindrance between the ABMA monomers (Scheme 2).

To investigate the effect of the molecular polarity on the reactive double bond, and the relative reactivity of the comonomers, r_1 and r_2 for poly (ABMA-co-MMA) and poly (ABMA-co-St) and Q and e values for ABMA were estimated. The monomer reactivity ratios (r_1, r_2) for the copolymers were calculated according to the method of Fineman–Ross.[14] Q and e values were calculated by assuming that Q and e values for MMA and St were 0.74, 0.4 and 1.0, −0.8, respectively.[15] The results are summerized in Table II. As can be seen in Table II, the $r_1 r_2$ value of poly (ABMA-co-St) is much smaller than that of poly (ABMA-co-MMA). This result suggests that the copolymerization of poly (ABMA-co-St) is more like an alternating system as compared with that of poly (ABMA-co-MMA), which is in accordance with the observed compositions shown in Table I (entries 2 and 3).

The monomer feed dependence, temperature, and time effects on the copolymerization of ABMA with MMA were investigated, and the results are summarized in Figures 1–4. As can be seen in the figures, the polymer conversion increased with increasing the reaction time and/or temperature. The specific rotation of the copolymer increased with increasing the chiral ABMA unit contained in the copolymer, which was dependent on feeding concentraction.

The temperature dependencies and solvent effects on the specific rotation for the ABMA monomer, homopolymer, and copolymers were investigated. As illustrated in Figure 5, a temperature dependence on the specific rotation was observed over the range 0–60°C. The values of the temperature coefficient ($\Delta[\alpha]/\Delta T$) for the systems were all smaller than
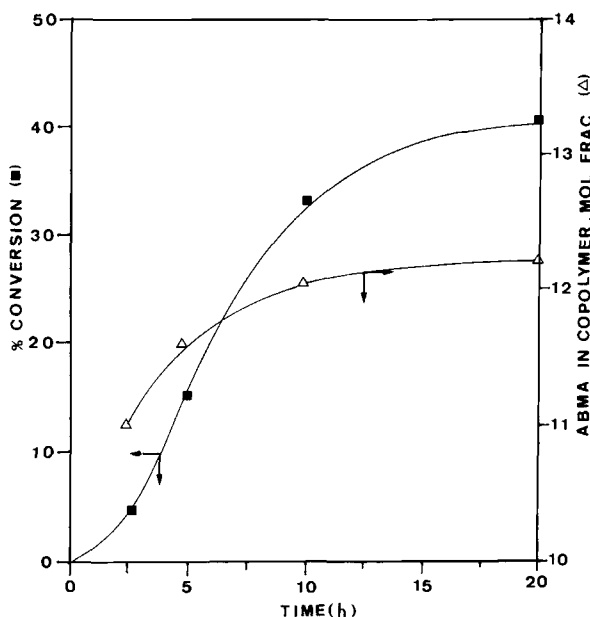
Table II Monomer Reactivity Ratio (r_1, r_2) for Poly(ABMA-co-MMA) and Poly(ABMA-co-St), and Q_1 and e_1 Values for ABMA[a]

M_1	M_2	r_1[b]	r_2[b]	Q_1[c]	e_1[c]	$r_1 r_2$
ABMA	MMA	0.32	3.08	0.37	0.52	0.98
ABMA	St	0.20	0.89	0.39	0.51	0.18

[a] In benzene at 60°C with 1 wt % AIBN.
[b] By Fineman–Ross method.[14]
[c] Q^2 and e^2 values for MMA and St are 0.74, 0.4, and 1.0, −0.8, respectively.[15]
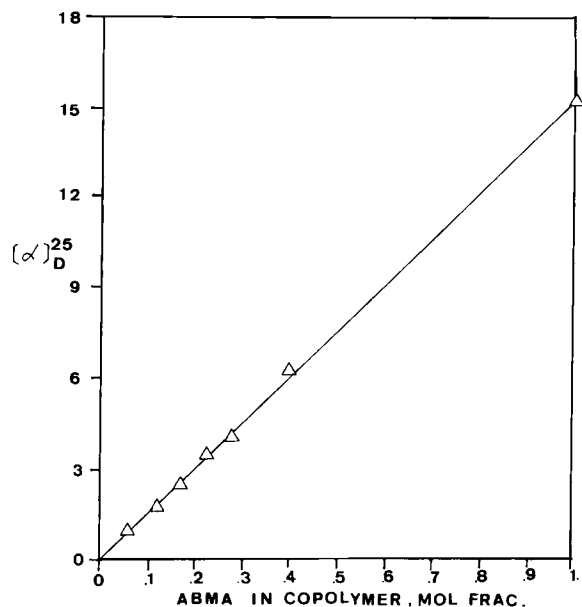

Figure 1 Time effect on the copolymerization of ABMA with MMA. Feed monomers: mol % of ABMA = 26.3, benzene = 5 mL, at 60°C, AIBN = 1 wt % of total monomers; (■) % conversion; (△) ABMA in copolymer mol fraction.

−0.1. The solvent dependencies on the specific rotation for ABMA–MMA and ABMA–St copolymers were observed, as shown in Figure 6. The specific rotation for the copolymers decreased linearly with increasing the amount of THF. As pointed out by
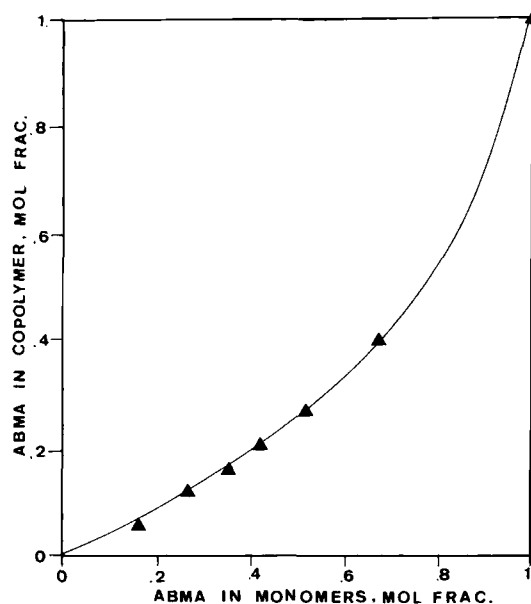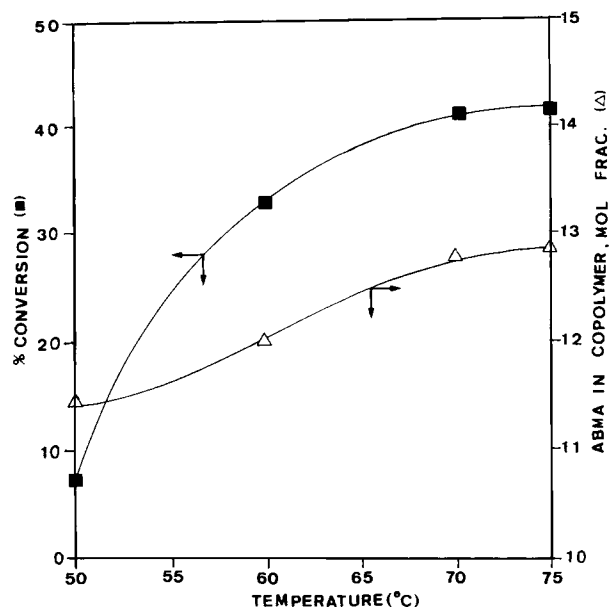

**Figure 2** Composition curve for poly (ABMA-co-MMA).

Figure 3 Plot of the specific rotation vs. ABMA content of poly(ABMA-co-MMA), at 60°C for 20 h.

Oishi et al.,[15,16] the results suggest that the helical conformation in the homopolymer and copolymers may not present.

To investigate the catalytic effect of the chiral polymers on the asymmetric induction, the asym-

Figure 4 Temperature effect on the copolymerization of ABMA with MMA. Feed monomer: mol % of ABMA = 26.3, benzene = 5 mL, for 10 h; AIBN = 1 wt % of total comonomers; (■) % conversion; (△) ABMA in copolymer mol fraction.
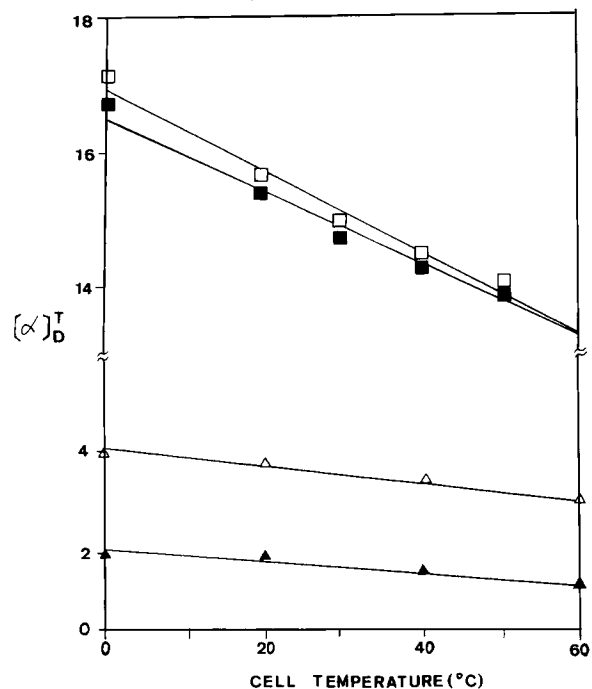

Figure 5 Temperature dependence on the specific rotation $[\alpha]_D$ (c = 0.05 g/mL, THF); (■) ABMA monomer; (□) PABMA; (▲) poly(ABMA-co-MMA); (△) poly(ABMA-co-St).

metric addition of n-butyllithium to aldehydes was carried out in the presence of chiral polymers containing acetoxybornyl groups. Table III shows the results of the asymmetric induction of n-butyl-lithium with various aldehydes in the presence of chiral polymer (7) as catalyst.

Generally, decreasing the reaction temperature leads to higher enantioselectivity; however, with some low molecular weight models, to a decrease of the yield.[18-21]

For asymmetric induction in the presence of a polymer, the enantiomeric excess was found to increase with the reaction temperature. The highest enantiomeric excess (51.3%) was achieved at 10°C. This indicates that the linear chiral polymer (7) provides an effective chiral environment and the enantioselectivity occurs effectively at 10°C. At higher reaction temperature, the enantiomeric excess appears to decrease. This result may suggest that the complex formed during the reaction is unstable at higher temperatures.

At higher temperatures, the polymer chain may expand and thus provide space to form complexes with ligands. Thus, each optically active site of the chiral catalyst is more accessible to the reactants and the asymmetric induction occurs effectively
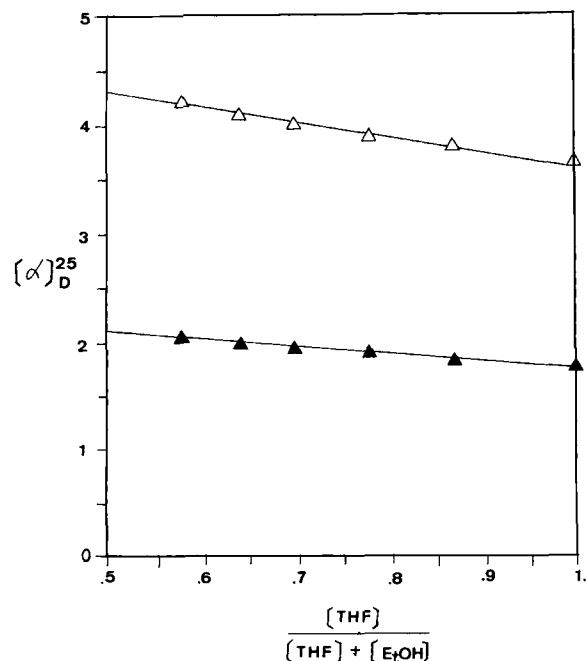
Figure 6 Solvent effect on the specific rotation $[\alpha]_D$ (0.05 g/mL, THF). (▲) poly(ABMA-co-MMA); (△) poly(ABMA-co-St).

within the polymeric chiral environment. At higher temperature, however, the stability of the complex tends to decrease. At lower temperatures, a greater number of reactions may occur under achiral environment without effective chiral induction of the chiral catalyst.

Generally, the immobilization of the asymmetric catalysts frequently lowers the optical yields in comparison to those obtained in the homogeneous low molecular weight system. The reason is not specified in detail, but the inefficiency is presumed to be related to the steric crowding and/or to the reaction environment in the polymer resin phase. The configuration of the products was determined by comparing the sign of rotation described in the literature. A schematic juxtaposition responsible for the enantioselectivity is shown in Scheme 3. Some coordination complex might be formed during the asymmetric addition that gave a relatively low optical yield, different from the case of low molecular weight models in which a more stable complex is considered.[22-24]

The polymeric catalyst can be recovered quantitatively by a simple filtration technique and could

Table III Conditions and Results of Asymmetric Additions of n-Butyllithium to Aldehydes Using the Chiral Polymer (7) as Catalyst[a]

Entry	Aldehydes	Temp (°C)	Yield[b] (%)	$[\alpha]_D^{30}$ (c,g/mL)[e]	e.e.% (Configuration)
1		20	65	+14.87 (3.12)	47.5 (R)[e]
2		10	72	+16.06 (4.10)	51.3 (R)
3	C_6H_5CHO	0	57	+14.65 (3.17)	46.8 (R)
4		−10	62	+13.87 (3.96)	44.3 (R)
5		−20	70	+13.02 (4.12)	41.6 (R)
6		−40	67	+12.11 (3.75)	38.7 (R)
7	$C_6H_{11}CHO$	10	75	+6.75 (4.12)	53.6 (R)[f]
8	$(CH_3)_2CHCHO$	10	72	+15.87 (4.06)	5.75 (R)[g]
9		10	68	+15.82 (3.68)	57.3 (R)[h]

[a] Mol ratio of aldehyde/BuLi/polymer = 1/1.2/1.5.
[b] Isolated chemical yield.
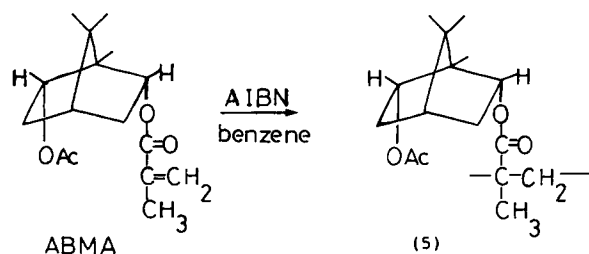[c] Solvent; benzene.
[d] Based on $[\alpha]_D$ =1 +31.3.[17]
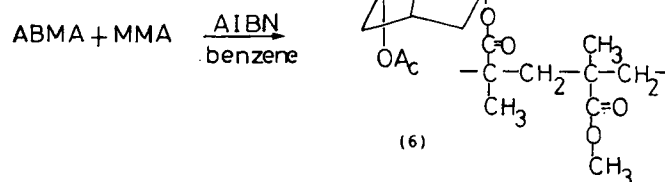[e] Based on $[\alpha]_D$ = +12.6.
[f] Derivative alcohols.
[g] Based on $[\alpha]_D$ = +27.6.
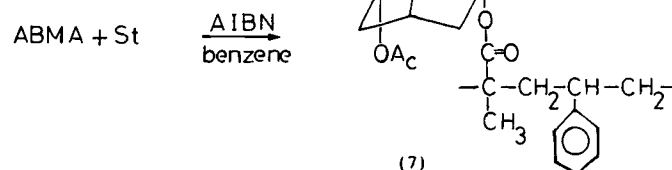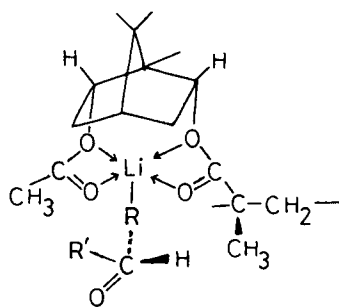[h] By recovered chiral polymer.

Homopolymerization :

ABMA $\xrightarrow[\text{benzene}]{\text{AIBN}}$ (5)

Poly(ABMA - co - MMA) :

ABMA + MMA $\xrightarrow[\text{benzene}]{\text{AIBN}}$ (6)

Poly(ABMA - co - St) :

ABMA + St $\xrightarrow[\text{benzene}]{\text{AIBN}}$ (7)

Scheme 2

R = n-Butyl
R'CHO = Aldehydes

Scheme 3

be reused for the further asymmetric addition without causing a decrease in enantiomeric excess. A further study of the effect of temperature on stability of the complex by spectroscopy is now in progress.

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