

Synthesis and Polymerization of 3-Oxobornyl Methacrylate

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SYNOPSIS

The new chiral monomer 3-oxobornyl methacrylate (OBMA) was synthesized from (+)-camphor. Homopolymerization of OBMA and copolymerization of OBMA with styrene were carried out in benzene in the presence of AIBN. The effect of concentration, solvent, temperature, and reaction time on the copolymerization were investigated. It was found that the absolute value of the specific rotation of poly(OBMA-*co*-St) increased by increasing the OBMA 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 polymers were investigated. The results suggest that chiral polymers contain no helix conformation. Inspecting the spectra of optical rotatory dispersion and circular dichroism, we found that the chiral polymers exhibit a strong negative Cotton Effect around 310 nm. © 1996 John Wiley & Sons, Inc.

INTRODUCTION

Optically active compounds have attracted great attention because living systems are chiral. Proteins and nucleic acids process chiral characteristic structures that are related closely to their functions. Because of chirality, living organisms usually show different biological responses to one or the other of a pair of enantiomers or optical isomers whether they are drugs, pesticides, or wastes.

Synthesis of chiral compounds from achiral reagents always yields the racemic modification. This is simply one aspect of the more general rule: Optically inactive reagents yield optically inactive products. Optically inactive racemates, however, can be separated in the chiral environment. A wide variety of polymeric chiral stationary phases (CSP) have been developed for the separation of enantiomers by means of high-performance liquid chromatography (HPLC).¹⁻⁴

During the course of our investigations on the synthesis of both monomers and polymers containing chiral groups derived from (+)-camphor, it was found that polymers with pendant chiral bornyl groups are effective for asymmetric induction re-

actions.⁵⁻⁷ In our previous paper, we synthesized chiral polymers poly(CPO-*co*-TDI) and poly(CPO-*co*-IPDI) from (+)-camphor and studied their applications on the optical resolution by the HPLC technique.⁸ In connection with studies on the catalytic functionality of chiral polymers having bornyl moieties, the synthesis and polymerization of a new chiral monomer 3-oxobornyl methacrylate (OBMA) were studied.

This article describes synthesis of the optically active OBMA monomer from (+)-camphor and its polymerization under various conditions. Effects of temperature, concentration, and solvent on the polymerization were investigated. The optical activity and stereo characteristics of the chiral polymers were also investigated.

EXPERIMENTAL

Measurement

Infrared (IR) spectra were recorded on a Jasco VALOR III FT-IR spectrophotometer. Nuclear magnetic resonance (NMR) spectra were performed on a Bruker-100, high-resolution NMR spectrometer. Ultraviolet (UV) spectra were recorded on a Jasco 7850 UV/VIS spectrophotometer. Optical rotations were measured at 30°C using a Jasco DIP-

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Table I Concentration Effect of Copolymerization

Entry	Feed OBMA (mol %)	Chiral Copolymer		
		C-analysis ^a (%)	OBMA ^a (mol %)	$[\alpha]_D^b$
1	20	80.14	37.35	-9.7
2	30	76.51	56.55	-13.8 ^c
3	50	73.71	76.36	-18.0
4	70	72.76	84.47	-21.1
5	100	71.18	100.00	-24.2 ^d

Copolymerization of OBMA with styrene in 5 mL benzene; AIBN = 1 wt % of total comonomers at 60°C for 18 h.

^a Estimated from elemental analysis.

^b C = 0.1 mg/mL in CHCl₃.

^c Molecular weight = 1.2×10^5 , evaluated by GPC.

^d Molecular weight = 5.7×10^4 , evaluated by GPC.

360 automatic digital polarimeter with readings to $\pm 0.001^\circ$. Elemental analyses were calculated with a Heraeus CHN-O rapid elemental analyzer. Circular dichroic (CD) spectra of the chiral polymers were measured with a Jasco J-720 spectropolarimeter. A Hitachi L-4200 UV/VIS high-performance liquid chromatograph was used.

Preparation

Camphorquinone (2)

Selenium dioxide (50 g) was added to the mixture of (+)-camphor (1) (42 g) in 45 mL of acetic anhydride, and then refluxed at 145°C for 7.5 h. After the reaction, the selenium was filtered off and washed with acetic acid. The filtrate was neutralized with a cold saturated potassium hydroxide solution in an ice bath. A large amount of yellow precipitate

was obtained during the neutralization. After filtration, the crude product was recrystallized from petroleum benzene. Yield: 84.2%. $[\alpha]_D = -107.4^\circ\text{C}$ ($c = 10$ mg/mL, DMF); FT-IR (KBr): 1748 cm^{-1} (C=O). ¹H-NMR (Acetone-d₆): $\delta = 0.88, 1.04, 1.08$ ppm (*m*, 9H, —CH₃); $\delta = 1.58-2.23$ (*m*, 4H, —CH₂—); $\delta = 2.59, 2.60$ ppm (*d*, 2H, —CH—).
C₁₀H₁₄O₂ (166.2): Calc C 72.26 H 9.49
Found C 72.32 H 8.45

Camphorquinone-3-ethylene ketal (3)

Camphorquinone (2) (10 g) was refluxed with 7.5 g of ethylene glycol in 200 mL of benzene in the presence of 0.5 g of *p*-toluenesulfonic acid for 30 h using Dean-Stark equipment. The reaction mixture was washed with dilute sodium hydroxide solution and water, then it was dried over magnesium sulfate and evaporated. The residue was recrystallized from pe-

Table II Time Effect on the Copolymerization

Entry	Feed OBMA (mol %)	Time (h)	Chiral Copolymer		
			Conversion (%) ^a	OBMA Content (mol %) ^b	$[\alpha]_D^c$
1	30	6	15.26	37.85	-10.1
2	30	12	28.85	47.15	-12.0
3	30	18	40.07	56.55	-13.8 ^d
4	30	24	44.48	58.76	-15.1

Copolymerization of OBMA with styrene in 5 mL benzene; AIBN = 1 wt % of total comonomers at 60°C.

^a (Weight of polymer/total weight of monomers) $\times 100\%$.

^b Estimated from elemental analysis.

^c C = 0.1 mg/mL in CHCl₃.

^d Molecular weight = 1.2×10^5 , evaluated by GPC.

Table III Temperature Effect on the Copolymerization

Entry	Feed OBMA		Chiral Copolymer		
	(mol %)	Temp (°C)	Conversion (%) ^a	OBMA Content (mol %) ^b	$[\alpha]_D^c$
1	30	60	40.07	56.55	-13.8 ^d
2	30	65	45.58	64.12	-16.0
3	30	70	48.21	73.74	-17.5
4	30	75	49.50	79.01	-19.8

Copolymerization of OBMA with styrene in 5 mL benzene; AIBN = 1 wt % of total comonomers.

^a (Weight of polymer/total weight of monomers) × 100%.

^b Estimated from elemental analysis.

^c C = 0.1 mg/mL in CHCl₃.

^d Molecular weight = 1.2 × 10⁵, evaluated by GPC.

troleum ether/benzene; colorless prisms were obtained (mp 89°C). Yield: 6.7 g (53%). $[\alpha]_D = +52.6^\circ$ (C = 1.2 cg/mL; in benzene). FT-IR (neat): 1750 cm⁻¹ (C=O), 1030, 1050 cm⁻¹ (C—O). ¹H-NMR (CDCl₃): $\delta = 0.90, 0.98, 1.02$ ppm (*m*, —CH₃, 9H); $\delta = 1.50\text{--}2.07$ ppm (*m*, 5H); $\delta = 3.80\text{--}4.38$ ppm (*m*, 4H).

C₁₂H₁₈O₃ (210.3): Calc C 68.57 H 8.57
Found C 68.42 H 8.55

(-)-2-Exo-Hydroxy-3-bornanone (4)

The ketal (3) (10 g) in 70 mL of ether/methanol (vol ratio 1 : 1) was cooled to about 0°C in an ice bath, and sodium borohydride (1.8 g) was added to it. The mixture was stirred in an ice bath for 30 min. After an exothermic reaction, the mixture was kept at 0°C for 2.5 h longer. The reaction mixture was washed several times with water, and ether was evaporated,

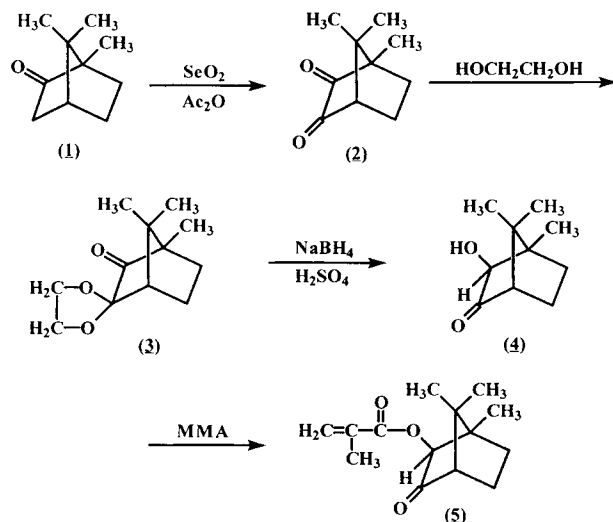
leaving an oil which was cooled to about 5°C and mixed with 20 mL of ice-cold concentrated sulfuric acid/water (vol ratio 1 : 1). After 15 min, 10 g of ice was added, and the mixture was extracted several times with ether. The ether was evaporated, and the residue was recrystallized from hexane. The product was further purified by column chromatography (Wako gel C-200). Mp 224°C in a sealed tube. Yield: 5.2 g (65%). $[\alpha]_D = -125.5^\circ$ (c = 2.1 mg/mL, benzene); FT-IR (KBr): 3600 cm⁻¹ (—OH) and 1750 cm⁻¹ (C=O); ¹H-NMR (CDCl₃): $\delta = 3.52$ ppm (*s*, 1H, 2-endo-H); $\delta = 0.89, 0.94, 1.02$ ppm (*m*, —CH₃, 9H); $\delta = 1.35\text{--}2.02$ ppm (*m*, 5H); $\delta = 2.17, 2.19$ ppm (*d*, 1 H, OH).

C₁₀H₁₆O₂ (168.2): Calc C 71.42 H 9.52
Found C 71.32 H 9.47

3-Oxo-bornylmethacrylate (5)

A mixture of (-)-2-exo-hydroxy-3-bornanone (4) (8 g), methacrylic acid (5 g), and *p*-toluenesulfonic acid (1.5 g) was heated in 200 mL of benzene at 100°C in the presence of hydroquinone (3 g). Water, liberated during the reaction, was removed by a Dean-Stark apparatus for 20 h. After completion of the reaction, the resulting mixture was washed with dilute aqueous sodium hydrogen carbonate solution and then with water. The oily layer was separated, dried over anhydrous magnesium sulfate, and distilled in vacuum to yield the product; bp 93°C/1 torr. Yield: 63%. $[\alpha]_D = -42.34^\circ$ (c = 0.5 mg/mL, benzene); FT-IR (neat): 1730, 1760 cm⁻¹ (C=O), 1640 cm⁻¹ (C=C). ¹H-NMR (CDCl₃): $\delta = 0.88, 0.93, 1.01$ ppm (*m*, —CH₃, 9H); $\delta = 4.88, 4.94$ ppm (*d*, 1H, 2-endo-H); $\delta = 5.61, 6.12$ ppm (each *s*, 1H, C=CH₂); $\delta = 1.95$ ppm (*s*, 3H, C=C—CH₃).

C₁₄H₂₀O₃ (236): Calc C 71.18 H 8.47
Found C 71.22 H 8.49



Scheme 1

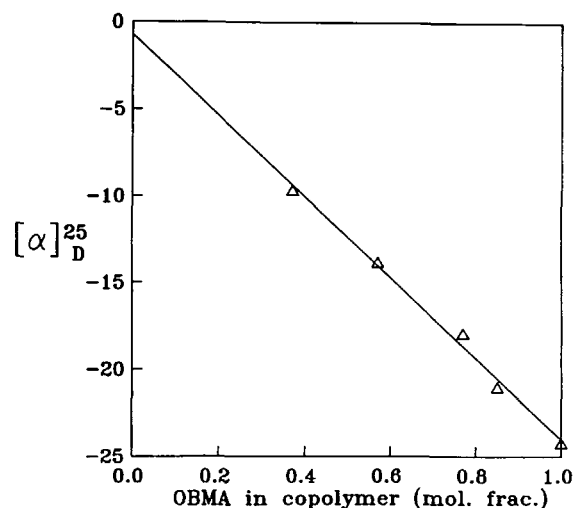


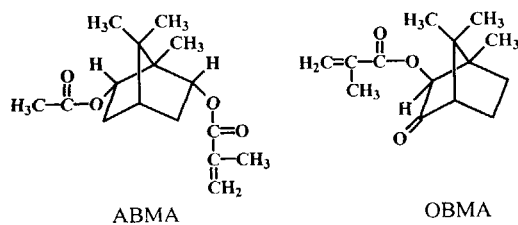
Figure 1 Dependence of specific rotation on OBMA content of poly(OBMA-co-St), at 60°C for 18 h.

Polymerization of the Chiral Monomer

Chiral polymers were prepared in various solvents. The monomer, solvents, and AIBN (2,2-azobisisobutyronitrile) were added in the above order into a polymerization tube, which was degassed in vacuum by using 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 chiral polymers. The crude polymers were purified by reprecipitation using benzene/methanol as nonsolvents. The conversion was calculated by gravimetry. Copolymerization of the chiral monomer (OBMA) with the achiral comonomer of styrene (St) was carried out in various solvents for a certain polymerization time. The results of the homopolymerization and the copolymerization are summarized in Tables I, II, and III.

RESULTS AND DISCUSSION

Camphorquinone (2) was synthesized from (+)-camphor in the presence of selenium dioxide as



Scheme 2

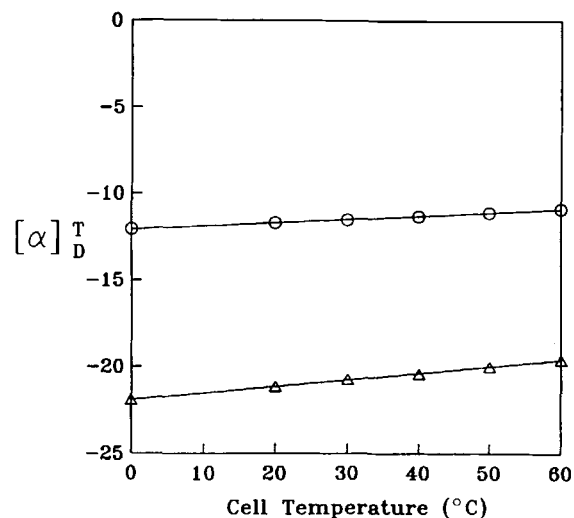


Figure 2 Temperature dependence on the specific rotation $[\alpha]_D$ ($c = 0.1$ mg/mL). Δ , poly(OBMA); \blacktriangle , poly(OBMA-co-St).

shown in Scheme 1. The carbonyl group on position 3 was protected by the introduction of a ketal structure. The ketal (3) was then treated with sodium borohydride and acid aqueous solution to produce the product of (-)-2-*exo*-hydroxy-3-bornanone (4). Esterification of hydroxy bornanone (4) with methacrylic acid led to the production of the new chiral monomer 3-oxo-bornylmethacrylate (5). Specific rotations of the chiral compounds were evaluated at 30°C using a Jasco DIP-360 automatic digital polarimeter with readings to $\pm 0.001^\circ$. Structures of the synthesized compounds shown in Scheme 1 were all confirmed by elemental analysis, $^1\text{H-NMR}$, and

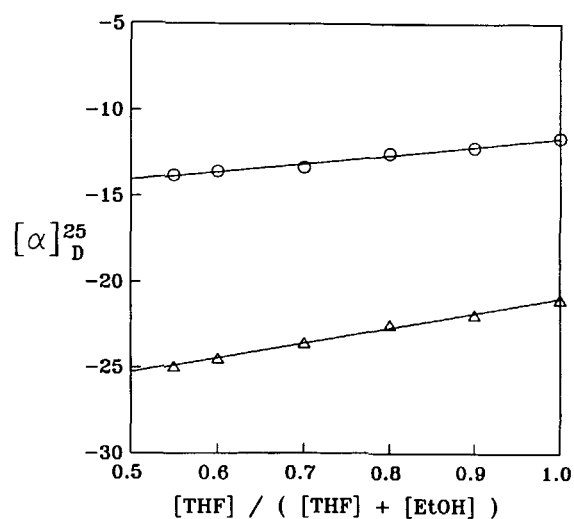


Figure 3 Solvent effect on the specific rotation $[\alpha]_D$ ($c = 0.1$ mg/mL). Δ , poly(OBMA); \blacktriangle , poly(OBMA-co-St).

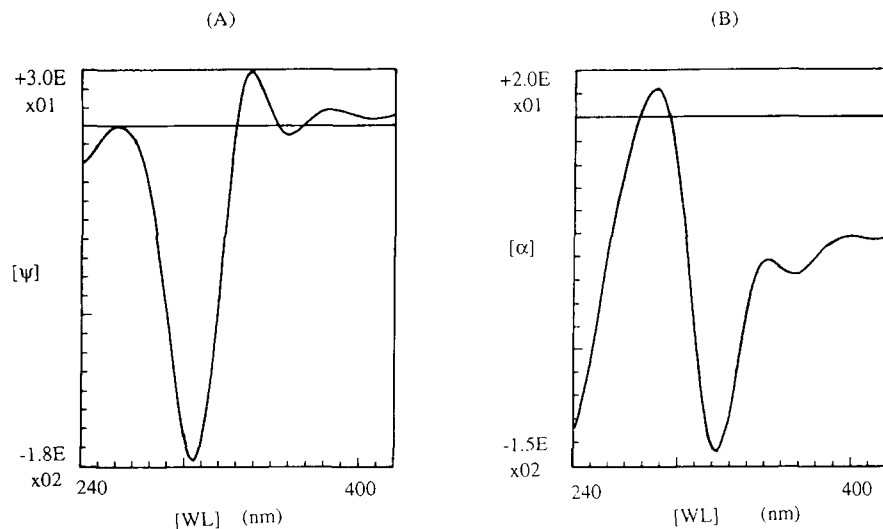


Figure 4 CD (A) and ORD (B) spectra of OBMA.

FT-IR spectroscopy. The $^1\text{H-NMR}$ signal of the endo-hydrogen in position 2 of the compound (4) showed the same chemical shift as those described in the literature.⁹ The result suggests that the carbonyl group at the C (2) position of the chiral compound (3) was reduced stereoselectively.

Homopolymerization of the new chiral monomer 3-oxo-bornyl methacrylate (5) and the copolymerization of the chiral monomer with achiral styrene (St) were carried out in various conditions. The results are summarized in Tables I–III. As shown in Table I, the specific rotation of the polymers increased with increasing the content of chiral unit in

polymers. The content of chiral unit was estimated by elemental analysis. The dependencies of chiral unit content on the specific rotation for polymers are shown in Figure 1. The specific rotation for the copolymers increased linearly with increasing the amount of OBMA unit. As pointed out by Oishi et al.,^{10,11} the results suggest that the chiral center may not be induced in the polymer main chain.

Effects of temperature and reaction time on the polymerization were also investigated. As can be seen in Tables II and III, the conversion and specific rotation are all increased with increasing temperature and reaction time. Conversions ob-

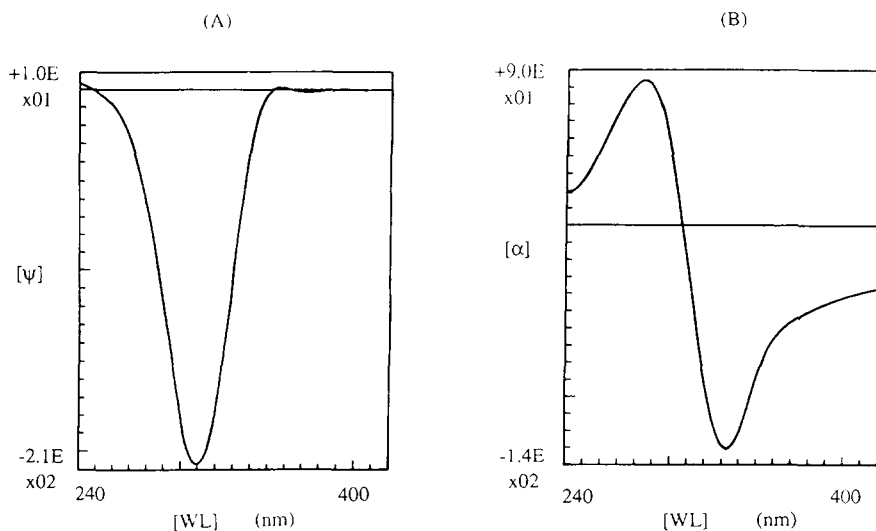


Figure 5 CD (A) and ORD (B) spectra of poly(OBMA).

tained here are all greater than those described in our previous paper, the synthesis and polymerization of 2-*endo*-acetoxy-6-*endo*-bornyl methacrylate (ABMA).¹² This result suggests that the steric hindrance of the ABMA seems to be greater than that of OBMA. As can be seen in Scheme 2, the acetoxy and the methacrylyl groups of the OBMA are all attached in the *endo* position. Only one methacrylyl group, however, existed in ABMA, and the group is attached in the *exo* position.

The temperature dependencies and solvent effects on the specific rotation for the POBMA and poly(OBMA-*co*-St) were investigated. As illustrated in Figure 2, temperature dependencies of the specific rotation were observed over the range of 0–60°C. The values of the temperature coefficient ($\Delta[\alpha]/\Delta T$) for the systems were all small. The solvent dependencies of the specific rotation for polymers are shown in Figure 3. The specific rotation for the copolymers increased linearly with increasing amount of THF. The results suggest that the helical conformation in the chiral polymers may not present.

To get further information on the stereo structure of the chiral polymers, a comparison of the CD and ORD spectra of the chiral monomer and chiral polymers was carried out. As can be seen in Figures 4–5, CD and ORD spectra of chiral polymers were comparable to that of chiral monomer. The same negative Cotton Effect can be found around 310 nm. These results suggest that chiral polymers poly(OBMA) and poly(OBMA-*co*-St) may have no one-handed helix conformation. These results are consistent with those described previously in Figures 2 and 3. The application of the chiral polymers to asymmetric induction is now in progress.

CONCLUSION

Chiral monomer OBMA (5) can be synthesized from (+)-camphor. The chiral center may not be induced

in the polymer main chain of poly(OBMA) and poly(OBMA-*co*-St). The steric hindrance of the ABMA seems to be greater than that of OBMA. From the results of the solvent and temperature effects on the specific rotation of the chiral polymers, it was found that chiral polymers poly(OBMA) and poly(OBMA-*co*-St) may have no one-handed helix conformation. The results are consistent with those obtained by the CD and ORD spectrophotometer.

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