Synthesis and Polymerization of Optically Active Mono-I-Menthyl Itaconate

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SYNTHESIS AND POLYMERIZATION OF OPTICALLY ACTIVE MONO-*l*-MENTHYL ITACONATE

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ABSTRACT

Optically active mono-*l*-menthyl itaconate (MMI) was prepared from itaconic acid and *l*-menthol. MMI was polymerized in bulk at 80°C to give a chiral homopolymer having −49.5° specific rotation. MMI (M_1) was copolymerized with styrene (ST, M_2), methyl methacrylate (MMA, M_2), and *N*-cyclohexylmaleimide (CHMI, M_2) by using 2,2′-azobisisobutyronitrile (AIBN) as the radical initiator and benzene as the polymerization solvent at 50°C. The monomer reactivity ratios (r_1, r_2) and Alfrey-Price Q, e values were determined to be $r_1 = 0.28$, $r_2 = 0.32$, $Q_1 = 0.90$, and $e_1 = 0.75$ in MMI–ST; $r_1 = 0.09$ and $r_2 = 0.51$ in MMI–MMA; and $r_1 = 0.78$ and $r_2 = 0.39$ in MMI–CHMI. The chiroptical properties of the polymers were investigated.

INTRODUCTION

Polymerizations and copolymerizations of mono- and dialkyl itaconates have been studied for many years [1]. There have been more than 20 reports lately, including patents, on itaconic acid and its esters [2]. Interest in these materials is due to their wide range of applications. For example, they are used on contact lenses and as antioxidants, coatings, binders, adhesives, copy materials, and films [3]. However, no investigation of the polymerization of optically active itaconates has been made with the exception of our report on the polymerizability and chiroptical properties of di-*l*-menthyl itaconate homopolymer and copolymers [4].

In this paper we report on the preparation of a novel optically active mono-*l*-menthyl itaconate (MMI) and its copolymerization with styrene (ST), methyl

methacrylate (MMA), or *N*-cyclohexylmaleimide (CHMI). The polymerizabilities and chiral properties of polymers and copolymers are described.

The final objective of this study is to find a useful chiral stationary phase, i.e., chiral packing for high performance liquid chromatography (HPLC), by using the polymers obtained from an unsaturated dibasic acid and its derivatives. In order to obtain some fundamental copolymerization parameters, Q and e values and monomer reactivity ratios, MMI was copolymerized with ST or MMA. In addition, since CHMI was a 1,2-disubstituted ethylene-type monomer, the copolymerization of a chiral monomer of MMI with CHMI may introduce asymmetry into the copolymer main chain. Consequently, the copolymer may have greater resolving characteristics for racemic compounds. Chromatographic resolution of racemic compounds will be reported in the near future.

EXPERIMENTAL

Monomer

MMI was synthesized from itaconic acid and *l*-menthol, as shown in Scheme 1. A mixture of 200 g (1.5 mol) itaconic acid, 250 g (1.6 mol) *l*-menthol, and 20 g *p*-toluenesulfonic acid in 750 mL benzene was refluxed for 24 h. A Dean-Stark tube was used to remove the water obtained in the reaction system. After completion, the reaction mixture was cooled to give crude MMI. The precipitate was filtered, washed with a small amount of benzene, dried, and then recrystallized from methanol–water (vol. 2:1) to give colorless crystals having a 77°C melting point, $[\alpha]_D^{20} = -54.3°$ ($c = 1.0\%$, THF): yield 75%.

IR (cm^{-1}): 1750 and 1730 (C=O), 1640 (C=C), 1200 and 1170 (COOR).

^{1}H-NMR (δ, ppm in CDCl$_3$): 10.9 (s, 1H) –COOH; 6.1 (d, J = 38 Hz, 2H), CH$_2$=C; 4.4–4.9 (m, 1H) –O–CH–; 3.3 (s, 1H) –CH$_2$COO–; 1.0–1.2 (m, 9H) menthyl –CH$_2$–; 0.85 (d, J = 1.2 Hz, 6H) (CH$_3$)$_2$C; 0.65 (s, 3H) CH$_3$C.

Elemental analysis (%): Found, C = 67.13, H = 9.02; calculated for C$_{15}$H$_{24}$O$_4$, C = 67.31, H = 9.38.

Styrene (ST) and methyl methacrylate (MMA) were purified by the usual
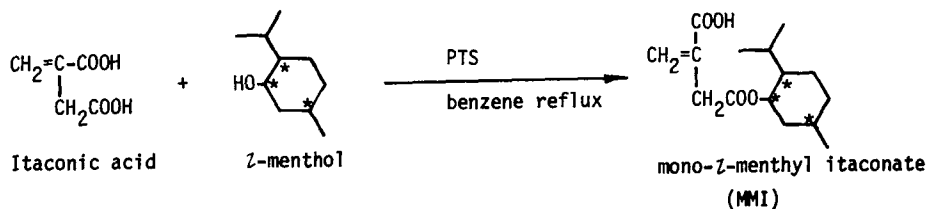
SCHEME 1.

methods. CHMI was prepared from maleic anhydride and cyclohexylamine [5]; mp 89°C.

Homopolymerization and Copolymerization

Radical homopolymerization and copolymerization were carried out with 2,2′-azobisisobutyronitrile (AIBN: mp 102°C) as an initiator in benzene and in bulk in sealed tubes at 50 (solution polymerization and copolymerization) and 80°C (bulk polymerization). After polymerization, the solution was poured into a large amount of petroleum ether which precipitated the polymer. To remove an unreacted optically active monomer, reprecipitation was repeated three times from THF–petroleum ether. The compositions of the copolymers obtained were determined by elemental analysis (C, H).

Measurements

D-Line specific rotations were measured with a Jasco DIP-140 (Japan Spectroscopic Co.). ORD and CD spectra were obtained with a Jasco J-20 (Japan Spectroscopic Co.) equipped with a xenon source and a computing data processor. A UV-200A spectrophotometer (Shimadzu Co.) was used to obtain spectra. The molecular weights of polymers and copolymers were measured by gel permeation chromatographic (GPC) analysis by using the same technique described in an earlier article [6]. IR and NMR spectra and elemental analysis were obtained by using the same instruments reported previously [7].

RESULTS AND DISCUSSION

Homopolymerization of MMI

Bulk and solution polymerizations of MMI were performed under several conditions summarized in Table 1. The solution homopolymerizations were unsuccessful, and the yields in the bulk polymerizations at 80°C with 1.0×10^{-1} mol/L of AIBN were only about 15 to 20%. The number-average molecular weight ($\bar{M}_n$) and weight-average molecular weight ($\bar{M}_w$) for poly(MMI) were about 1700 to 5500 and about 26 000, respectively. The specific rotation $[\alpha]_D^{20}$ was −49.5° ($c = 1.0$, THF, $l = 10$ cm). The optical rotary dispersion (ORD) was found to fit the simple Drude equation. In the circular dichroism (CD) spectrum for the homopolymer, a positive Cotton effect was observed at about 216 nm (the mean residue ellipticity: $[\theta]_{216}^{20} = 2470$ to 2630 deg·cm²/dmol). In addition, a very small CD peak, i.e., a negative Cotton effect, was observed at about 268 nm ($[\theta] = \sim -40$ deg·cm²/dmol), which was consistent with the negative specific rotation of the polymer ($[\alpha]_D = -49.5°$). Both the CD patterns were attributable to

TABLE 1. Solution and Bulk Polymerization of MMI[a]

Run	Solvent (mL)	AIBN ($\times 10^{-2}$ mol/L)	Polymerization temperature, °C	Yield, %	$\bar{M}_n$[c] $\times 10^{-3}$	$\bar{M}_w/\bar{M}_n$[c] $\times 10^{-4}$	$[\alpha]_D^{20}$,[d] degrees	$[\theta]_{216}^{20}$[e]
A-1	Benzene (4 mL)	1.0	50	trace	—	—	—	—
A-2	THF (4 mL)	1.0	50	trace	—	—	—	—
A-3	Benzene (4 mL)	3.0	80	trace	—	—	—	—
A-4	THF (4 mL)	3.0	80	trace	—	—	—	—
A-5	None	1.6[b]	80	trace	—	—	—	—
A-6	None	5.1[b]	80	14.7	5.53	2.9	-50.5	2470
A-7	None	10.0[b]	80	19.0	1.68	15.3	-49.5	2630

[a]MMI = 2 g, polymerization time = 48 h.
[b][AIBN]/[MMI] × 100 = wt/wt%.
[c]Determined by GPC.
[d]c = 1.0%; THF, l = 10 cm.
[e]deg·cm^2/dmol; c = 1.0%; THF, l = 1 mm.

$n \rightarrow \pi^*$ transition of the carbonyl chromophore, which could be detected in the case of di-*l*-menthyl itaconate (DMI) [4].

Copolymerization

Results of radical copolymerizations of MMI (M_1) with ST (M_2), MMA (M_2), or CHMI (M_2) in benzene (10 mL) at 50°C in the presence of AIBN (1.0×10^{-2}mol/L) are summarized in Table 2. The copolymerizations proceeded homogeneously throughout, and the polymers obtained were white powders and optically active. $\bar{M}_n$ for poly(MMI-*co*-CHMI) was smaller than those for other systems, as shown in Table 2. The reason for this may be that CHMI has considerable steric hindrance because of the 1,2-disubstituted ethylene structure. $\bar{M}_n$ for the copolymers of MMI systems were generally larger than those of the copolymers obtained from di-*l*-menthyl itaconate (DMI) with ST, MMA, or CHMI [4].

Copolymer-composition curves for poly(MMI-*co*-ST)s, poly(MMI-*co*-MMA)s, and poly(MMI-*co*-CHMI)s are shown in Fig. 1. Monomer reactivity ratios r_1 and r_2 were determined according to the Mayo-Lewis [8] method: $r_1 = 0.28$ and $r_2 = 0.32$ in the MMI (M_1)–ST(M_2) system; $r_1 = 0.09$ and $r_2 = 0.51$ in the MMI (M_1)–MMA (M_2) system; and $r_1 = 0.78$ and $r_2 = 0.39$ in the MMI (M_1)–CHMI (M_2)

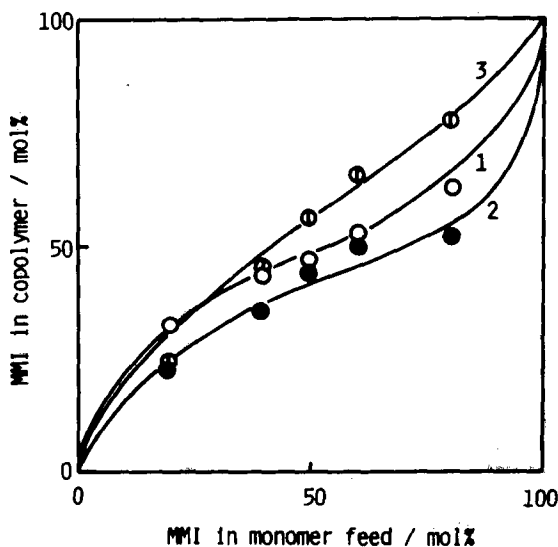FIG. 1. Copolymer-composition curves for (1) MMI (M_1)–ST (M_2), (2) MMI (M_1)–MMA (M_2), and (3) MMI (M_1)–CHMI (M_2).

TABLE 2. Radical Copolymerization of MMI (M_1) with ST (M_2), MMA (M_2), and CHMI (M_2) in benzene (10 mL) at 50°C[a]

Run	M_1 in monomer feed, mol%	M_2	Polymerization time, h	Yield, %	M_1 in copolymer, mol%	$\bar{M}_n \times 10^{-4}$	$\bar{M}_w \times 10^{-4}$	$[\alpha]_D^{20}$, degree
B-1	20.6	ST	10	8.0	32.5	9.5	21.8	-28.3
B-2	41.0	ST	10	9.8	43.7	7.9	20.0	-32.5
B-3	50.2	ST	10	11.2	46.5	5.6	13.7	-35.1
B-4	60.6	ST	10	10.3	52.9	4.4	17.5	-37.1
B-5	80.5	ST	10	6.5	62.5	4.4	12.7	-39.8
C-1	20.0	MMA	6	10.8	23.2	19.4	40.0	-22.7
C-2	39.9	MMA	6	10.4	35.5	19.0	42.4	-34.0
C-3	50.0	MMA	6	9.3	44.4	12.8	37.5	-37.4
C-4	60.0	MMA	6	7.7	49.9	8.8	34.4	-40.2
C-5	79.7	MMA	6	4.1	52.2	4.9	20.2	-42.3
D-1	19.3	CHMI	6	11.2	23.9	0.4	15.3	-13.7
D-2	39.9	CHMI	6	10.1	45.0	0.5	5.8	-26.2
D-3	49.6	CHMI	6	9.0	56.6	0.4	3.7	-33.7
D-4	60.1	CHMI	6	7.5	65.6	0.4	3.2	-37.3
D-5	79.9	CHMI	6	8.0	77.7	0.3	1.5	-41.5

[a] [AIBN] = 1.0×10^{-2} mol/L; $M_1 + M_2 = 5.0$ g; benzene = 10 mL.
[b] $c = 1.0\%$; THF; $l = 10$ cm.

system. The Alfrey-Price [9] Q-e values for MMI were calculated as $Q_1 = 0.90$ and $e_1 = 0.75$. These values suggest that MMI can be completely copolymerized with such crosslinking agents for the stationary phase of chromatography as ethylene diacrylate and ethylene dimethacrylate. These copolymerization parameters are similar to those for mono-*n*-butyl itaconate [10], mono-(2,2-dimethyl-1,3-dioxolan-4-ylmethyl) itaconate [11], and mono-(2-oxa-1,3-dioxolan-4-ylmethyl) itaconate [12]. This fact suggests that the copolymerizability could be slightly influenced by the ester substituent. In the case of disubstituted itaconate [4], the polymerizability was affected by the substituents. The reason for this may be the steric hindrance of the two substituents.

Optical Behavior of Copolymers

All poly(MMI-*co*-ST)s, poly(MMI-*co*-MMA)s, and poly(MMI-*co*-CHMI)s demonstrated negative optical activity as shown in Table 2. The absolute value of specific rotation of each copolymer increased with increasing MMI unit content and showed a practically linear dependence on the composition for the copolymer
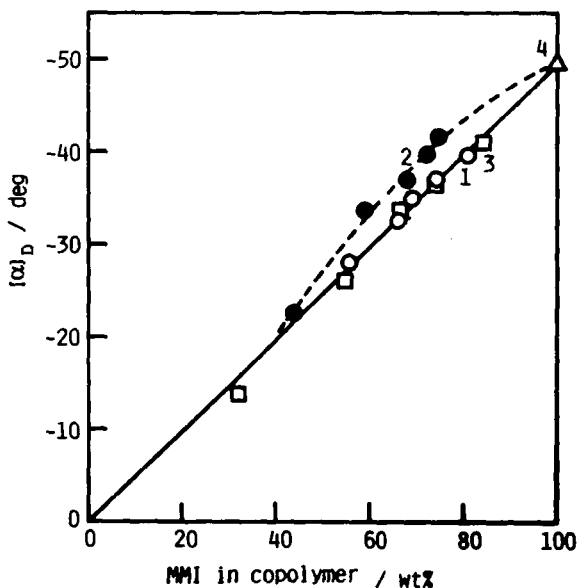

FIG. 2. Specific optical rotation at the sodium D-line versus composition for the system: (1) MMI–ST, (2) MMI–MMA, (3) MMI–CHMI, and MMI homopolymer (Run A-6).

as shown in Fig. 2. It has been reported that the specific optical rotation of copolymers comprising a chiral methacrylate with achiral vinyl monomers generally exhibit a nonlinear dependence on the copolymer composition [13]; an exception to this is the copolymer of *l*-menthyl methacrylate with styrene [14].

UV and CD curves of MMI homopolymer and the copolymers are shown in Fig. 3.

Large positive and small negative CD peaks for poly(MMI-*co*-ST) (Run B-2) are present at 226 and 268 nm, respectively. All the poly(MMI-*co*-ST)s showed small but well-defined CD peaks around 268 nm which are related to the lowest energy $\pi \rightarrow \pi^*$ transition (^1L_b) of the benzene chromophore. The magnitude of the observed ellipticity at 268 nm ($[\theta] = -27$ to -49 deg·cm²/dmol) reaches a maxi-
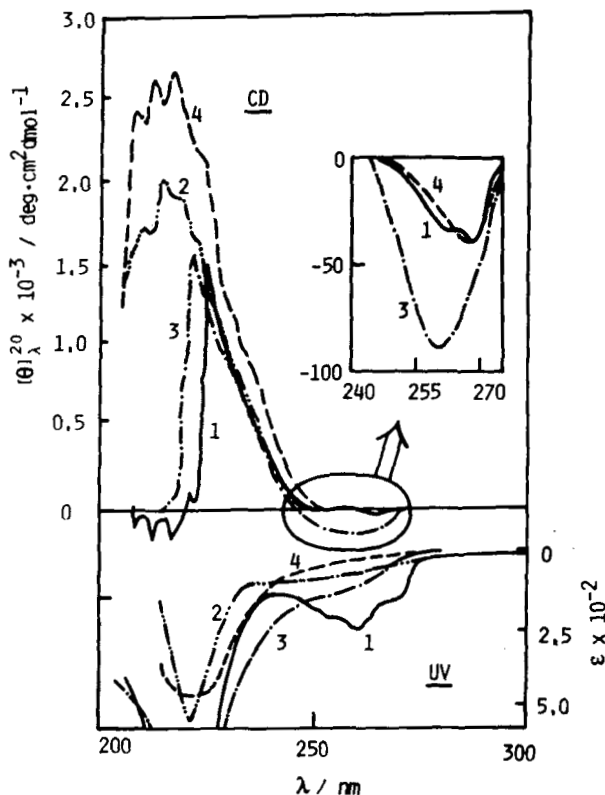

FIG. 3. UV and CD curves for (1) poly(MMI-*co*-ST) (Run B-2), (2) poly(MMI-*co*-MMA) (Run C-3), (3) poly(MMI-*co*-CHMI) (Run D-2), and (4) MMI homopolymer (Run A-7).
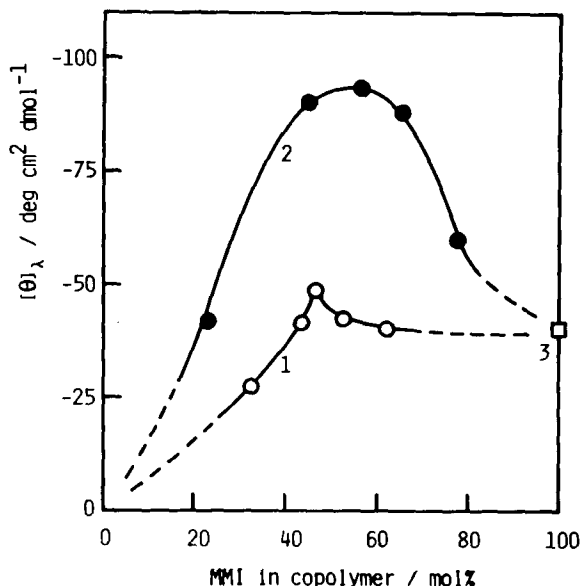
FIG. 4. Dependence of ellipticity [θ] on the composition of (1) MMI–ST ([θ] at 268 nm), (2) MMI–CHMI ([θ] at 260 nm), and (3) MMI homopolymer (Run A-6).

mum at about 45% MMI content which demonstrates that this comonomer can induce asymmetry in the MMI–ST system. Carlini et al. reported that a stereoregular copolymer of an achiral monomer with a chiral comonomer may exhibit induced optical activity of the nonchiral co-unit due to preferential chirality of the main chain [14]. When the nonchiral unit has an aromatic group in the side chain, the π→π* electron transition of the aromatic chromophore is optically active, even if the chiral (*l*-menthyl) group is at the δ-position from the main chain. It is interesting to note that induced asymmetry can be observed in our MMI–ST system in spite of the almost linear relation between $[\alpha]_D$ and the content (wt%) of MMI in the copolymer (Fig. 2). This observation for the MMI–ST system may also correspond to the previously reported exceptional observation for the case of the copolymerization of *l*-menthyl methacrylate with styrene [14]. In poly(MMI-*co*-ST)s, the mean residue ellipticities [θ] were 844 to 1490 deg·cm²/dmol at 226 nm, which may be due to n→π* transition of carbonyl groups of the MMI monomeric unit.

In the poly(MMI-*co*-MMA)s, the mean residue ellipticities [θ] at 218 nm were 1400 to 2610 deg·cm²/dmol, which may be attributed to n→π* transition of carbonyl groups in the copolymer. No other characteristic CD peaks could be

observed in the MMI–MMA system. However, a slight deviation from a straight line was detected, as shown in Fig. 2. The reason for this is difficult to explain. It is thought that the composition of the copolymer may not be as written as indicated by carbon analysis.

In poly(MMI-*co*-CHMI), UV and CD peaks were observed in the region of about 210 to 240 nm which corresponds to the n→π* transition of carbonyl groups in the MMI unit. A negative CD peak, i.e., the negative Cotton effect, was observed at about 260 nm and can be attributed to the n→π* transition of the carbonyl group in the imide ring. The magnitude of the observed ellipticity per maleimide residue at 260 nm is related to the MMI unit in the copolymer, as shown in Fig. 4. There have been no reports that the n→π* electron transition of the carbonyl group is optically active when the nonchiral unit has a carbonyl group in the side chain. Thus, the negative CD peak around 260 nm in the MMI–CHMI system can be attributed to a new asymmetric center in the copolymer main chain as described below. The values of ellipticity at 260 nm were plotted against the $P_2[m_1m_2]$ [15] values and indicated the probability of a MMI–CHMI diad sequence as shown in Fig. 5. An approximately linear relationship exists between the MMI–CHMI diad sequence and the ellipticity, which suggests that a new asym-
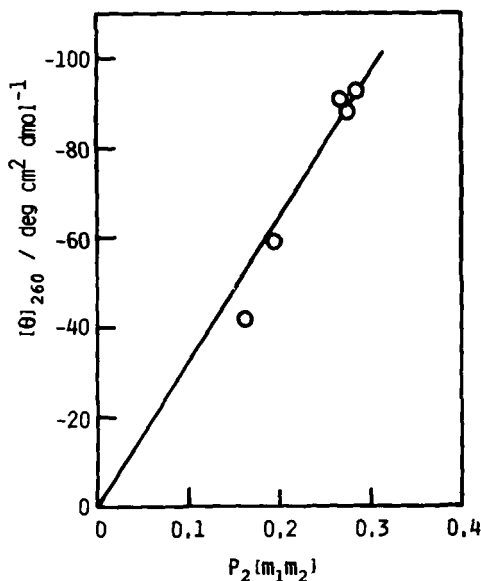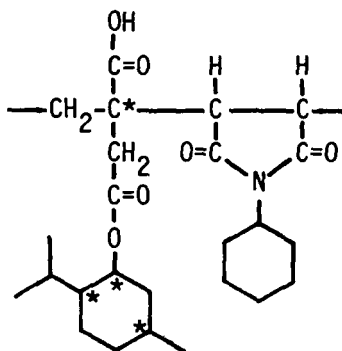

FIG. 5. Relationship between the ellipticity at 260 nm and the MMI–CHMI diad sequence for poly(MMI-*co*-CHMI)s.

metric center has appeared in the copolymer main chain as illustrated by

The asymmetric induction mechanism, as reported previously [16–18], may be explained by steric hindrance for the approach of CHMI monomer on the chiral chain end during the propagation reaction. Asymmetric induction copolymerizations were recognized in many cases between a chiral monomer and a 1,2-disubstituted ethylene-type monomer [19–22]. In the reverse case, that is, between an achiral monomer and a chiral 1,2-disubstituted ethylene monomer, they were also observed [16–18].

The temperature dependence on the specific rotation in all systems is nearly linear, as shown in Fig. 6. In addition, the absolute values of the temperature
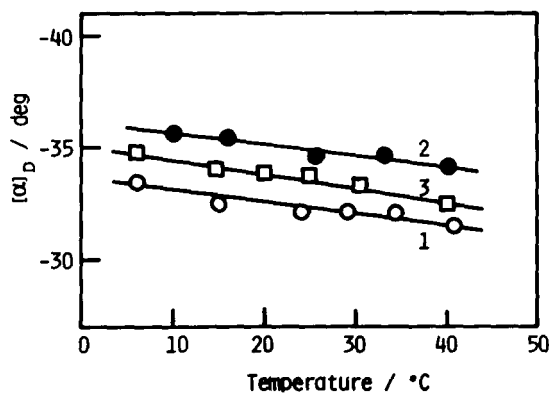
FIG. 6. Temperature dependence on specific optical rotation of the copolymer: (1) poly(MMI-*co*-ST) (Run B-3), (2) poly(MMI-*co*-MMA) (Run C-3), and (3) poly(MMI-*co*-CHMI) (Run D-3).

coefficient ($\Delta[\alpha]_D/\Delta T$) for all polymers were within 0.1. This suggests that no helix conformation exists in the copolymer.

CONCLUSION

1. A novel, optically active mono *l*-menthyl itaconate (MMI) was synthesized from *l*-menthol and itaconic acid. Homopolymerizations of MMI gave only trace amounts of polymer in solution and very small amounts of polymer in bulk at 80°C.

2. From the results of the radical copolymerization of MMI (M_1) with ST (M_2), MMA (M_2), or CHMI (M_2), monomer reactivity ratios (r_1, r_2) and Q-e values were determined as $r_1 = 0.28$ and $r_2 = 0.32$ (MMI–ST); $r_1 = 0.09$ and $r_2 = 0.51$ (MMI–MMA); $r_1 = 0.78$ and $r_2 = 0.39$ (MMI–CHMI), and $Q_1 = 0.90$ and $e_1 = 0.75$ for MMI.

3. In the MMI–ST system, an induced optical activity was observed around 268 nm, which was attributed to the aromatic chromophore in the side chain.

4. Asymmetric induction copolymerization took place in the MMI–CHMI system.

ACKNOWLEDGMENT

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