Exceptional chiroptical behavior near ceiling temperature in free radical polymerization of menthyl 2-acetamidoacrylates

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Abstract

Effect of polymerization conditions on chiroptical properties of polymer has been studied in the polymerization of ($-$)- and ($+$)-menthyl 2-acetamidoacrylates using radical initiators under the conditions with various temperatures, monomer concentrations, and reaction times. Specific rotation and circular dichroism of the resulting polymers indicated that a ceiling temperature (T_c) affected the chiroptical properties of the polymers and the polymerizations would give preferentially a helical polymer through a radical vinyl polymerization near T_c. In addition, the helical structure of the polymer was maintained intact even heating at 120 °C in anisole.
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1. Introduction

Optically active polymers have been prepared through asymmetric synthesis, enantiomer-selective and helix-sense-selective polymerizations mostly using an anionic initiator, and they have been interested in connection with their applications and mechanistic aspects [1]. Recently, however, synthesis of chiral polymers through a radical mechanism has attracted much attention since radical polymerization possesses some potential advantages, e.g. high accessibility for a number of monomers and solvents, high reproducibility, and easy procedures [2]. Among chiral vinyl polymers obtained via radical polymerization, a one-handed helical polymer is one of the most important and interesting polymer, but has only successfully been prepared through the polymerization of *N*-arylmethyl methacrylamides [3] and arylmethyl methacrylates [4] in the presence of chiral reagents such as menthol. In addition, unfortunately, consistent polymerization conditions that give rise to such a high stereoregular polymers have not yet been clarified.

1   **2**
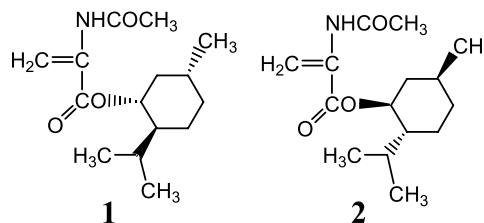
Recently, we found a characteristic chiroptical property, i.e. chiral helical conformation, of the polymers obtained by the radical polymerizations of **1** and **2** near the ceiling temperature (T_c) at which the propagation and depropagation rates become compatible (Eq. (1)). In the present study, we report a key condition that leads to a one-handed heat-resistant helical polymer from the radical polymerizations of **1** and **2**, which bear ($-$)- or ($+$)-menthyl ester and amide groups on the same carbon atom and can be expected to represent moderate polymerizability because of the captodative substitution effect [5] in spite of the bulky substitution.

$$\text{\raise.5ex\hbox{$\sim\!\!\sim\!\!\sim$}}M_n^\bullet + M \xrightarrow[\text{depropagation}]{\text{propagation}} \text{\raise.5ex\hbox{$\sim\!\!\sim\!\!\sim$}}M_{n+1}^\bullet \qquad (1)$$

2. Experimental

Basic chemicals were purchased from Wako Chemical Co. Azo initiators including 2,2′-azobis(isobutyronitrile)

(AIBN) and 1,1′-azobis (cyclohexane-1-carbonitrile) (ACHN) were purified by recrystalization from ethanol. Commercial grade 2,2′-azobis(4-methoxy-2,4-dimethylvaleronitrile) (AMVN) was used without further purification. Deuterated solvent including CDCl₃ used for NMR measurement was purchased from Acros Organics Co.

1 was prepared in 26.2% yield by refluxing acetamide and (−)-menthylpyruvate in benzene for 28 h in the presence of *p*-toluenesulfonic acid with removing water using Dean–Stark separator, in which (−)-menthylpyruvate was independently obtained by condensation of pyruvic acid and (−)-menthol in 80.6% yield in a similar manner to the above. **1** was purified by a column chromatography using a mixture of *n*-hexane and ethylacetate (4:1) as a developing solvent. **1** was obtained as a colorless oil, $[\alpha]_D = -81.2°$ in CHCl₃. ¹H NMR (CDCl₃, TMS, ppm): 0.76 (d, $J=7.1$ Hz, 3H, CH₃), 0.90 (d, $J=7.1$ Hz, 3H, CH₃), 0.92 (d, $J=6.6$ Hz, 3H, CH₃), 1.0–2.0 (m, 9H, menthyl), 2.13 (s, 3H, COCH₃), 4.80 (dt, $J=4.5$, 11 Hz, 1H, menthyl), 5.85 (s, 1H, CH=), 6.57 (s, 1H, CH=), 7.94 (br s, 1H, NH). Anal. Calcd for C₁₅H₂₅NO₃: C, 68.04; H, 9.41; N, 4.87. Found: C, 67.78; H, 9.42; N, 5.14. **2** was prepared according to the procedure similar to that of **1**, in which (+)-menthol was used instead of (−)-menthol, and purified by a column chromatography using a mixture of *n*-hexane and ethylacetate (4:1) as a developing solvent, $[\alpha]_D = +79.0°$ in CHCl₃. ¹H NMR (CDCl₃, TMS, ppm): 0.77 (d, $J=7.1$ Hz, 3H, CH₃), 0.90 (d, $J=7.1$ Hz, 3H, CH₃), 0.93 (d, $J=6.5$ Hz, 3H, CH₃), 1.0–2.0 (m, 9H, menthyl), 2.13 (s, 3H, COCH₃), 4.80 (dt, $J=4.5$, 11 Hz, 1H, menthyl), 5.85 (s, 1H, CH=), 6.57 (s, 1H, CH=), 7.80 (br s, 1H, NH). Anal. Calcd for C₁₅H₂₅NO₃: C, 68.04; H, 9.41; N, 4.87. Found: C, 67.85; H, 9.35; N, 5.02.

Polymerization was usually carried out in bulk, benzene, or toluene in a sealed ampoule with shaking at given temperature. The ampoule containing required amounts of reagents including initiator, solvent, and so forth was degassed several times by a freeze–thaw method and then sealed under reduced pressure and placed in a constant temperature bath. The resulting polymer was isolated by pouring the contents of the ampoule into a large amount of methanol. Overall polymerization rate (R_p) was determined by weighting an isolated polymer amount. Hydrolysis of polymer was carried out in the mixed solvent of benzene and methanol (1:2) containing KOH (5 wt%) for 5 h at 40 °C.

¹H NMR spectra were recorded on JEOL EX-400 (400 MHz) spectrometer at 20 °C in CDCl₃ for polymers **1** and **2** and in D₂O–KOH for a hydrolyzed polymer. Specific rotation $[\alpha]_D$ at $\lambda = 589.3$ nm (Na–D) was measured on JASCO DIP-360 digital polarimeter in CHCl₃ at ambient temperature. Circular dichroism (CD) was recorded on JASCO J-820 spectropolarimeter in *n*-hexane at 20–60 °C and *n*-heptane at higher temperature. Number-average molecular weight (M_n) of polymer was determined by size exclusion chromatography (SEC) using a Tosoh HLC 8020

(Column: TSKgel G7000HHR + G5000HHR + G3000HHR) in tetrahydrofuran at 35 °C on the basis of standard polystyrene.

3. Results and discussion

Polymerization of **1** was carried out using azo initiators including AIBN, AMVN, and ACHN in the conditions with various temperatures, monomer concentrations, and reaction times. As seen in Table 1, the specific rotation $[\alpha]_D$ of polymer **1** for Na–D line as well as the polymer yield varies with temperatures and monomer concentrations, and it is independent of the molecular weight (M_n) of polymer within these M_n region. For instance, the higher a monomer concentration is, the higher a polymerization feasible temperature is, and polymer **1** is not produced at 80 °C in $[\mathbf{1}] = 2.0$ mol L⁻¹, but even at 90 °C **1** gives a polymer in bulk polymerization, i.e. $[\mathbf{1}] = 3.7$ mol L⁻¹. In addition, the absolute $[\alpha]_D$ value of the resulting polymer tends to decrease with increasing polymerization temperature and that of the polymers obtained at 60 and 70 °C is lower than that obtained at 50 °C in $[\mathbf{1}] = 2.0$ mol L⁻¹, i.e. $[\alpha]_D = -77.0, -48.0$, and $-19.0°$ for the polymerization at 50, 60, and 70 °C, respectively. However, $[\alpha]_D$ value of the resulting polymer was little influenced by M_n of a polymer, e.g. $[\alpha]_D = -96.4, -77.2$ for $M_n = 3.79 \times 10^5, 3.50 \times 10^5$, and $[\alpha]_D = -48.0, -49.5°$ for $M_n = 1.07 \times 10^5, 2.88 \times 10^5$, respectively. These results suggest that depolymerization cannot be precluded in such a polymerization, for instance, at least in the 60–80 °C region in $[\mathbf{1}] = 2.0$ mol L⁻¹ and it competes with increasing temperature. It is noted, therefore, that T_c appears to play an important role in polymer chirality.

$$\ln (R_p k_d^{-0.5}[\text{initiator}]^{-0.5}[\text{monomer}]^{-1})$$
$$= \ln(A_p f^{0.5} A_t^{-0.5}) - (E_p - 0.5E_t)R^{-1}T^{-1} \qquad (2)$$

Fig. 1 shows a plot according to Eq. (2) [6], in which f and k_d denote initiator efficiency and decomposition rate constant, respectively, R is a gas constant, A and E are frequency factor and activation energy, respectively, T is absolute temperature, and subscripts p and t stand for propagation and termination processes, respectively. As seen in Fig. 1, such a plot displays a steep falling curve at higher temperature after giving a maximum value as often observed in the polymerization near T_c [7], and the slope of the curve approaches infinity at 75.4 °C which corresponds to T_c in benzene and $[\mathbf{1}] = 2.0$ mol L⁻¹. Similarly, T_c was estimated to be 58.5 and 98.0 °C for the polymerization in $[\mathbf{1}] = 1.0$ mol L⁻¹ and bulk, respectively [8], which strongly supports the dependence of the yield and specific rotation on T_c as seen in Table 1. That is, a negative value of $[\alpha]_D$ decreases along with approaching to T_c in bulk polymerization, e.g. $[\alpha]_D = -96.0, -49.5$, and $-42.6°$ for the polymerizations at 30, 80, and 90 °C, respectively.

Table 1
Polymerization of **1** at various temperatures in bulk and solution and polymer properties

Initiator[a]	[Monomer] (mol L^{-1})	Temperature (°C)	Time (h)	Yield[b] (%)	M_n[c] ($\times 10^{-4}$)	$[\alpha]_D$[d] (degree)
AMVN	1.0	30	10	37.4	16.7	−89.0
AMVN	2.0	30	10	82.5	37.9	−96.4
AIBN	2.0	50	10	50.2	35.0	−77.2
AIBN	2.0	60	20	40.1	10.7	−48.0
AIBN	2.0	70	6	5.7	1.43	−19.0
AIBN	2.0	80	2	0	–	–
AMVN	Bulk	30	10	32.2	–	−96.0
AIBN	Bulk	80	2	30.9	28.8	−49.5
ACHN	Bulk	90	8	0.5	0.76	−42.6
AIBN	Bulk	100	20	0	–	–

[a] [Initiator] $= 5.0 \times 10^{-3}$ mol L, abbreviations of AMVN, AIBN, and ACHN should be refered to text.
[b] Yield: yield of methanol-insoluble polymer.
[c] M_n: number-average molecular weight of polymer determined by size-exclusion chromatography at 35 °C in tetrahydrofuran using standard polystyrene.
[d] [Polymer] $= 0.2$ g dL^{-1} in CHCl$_3$ at ambient temperature.

Polymerization of **2** also gave a result similar to that of **1**, and $[\alpha]_D = +99.0, +47.6$, and $+35.4°$ were determined for polymer **2** obtained at 30, 60, and 70 °C, respectively, and T_c for **2** was estimated to be the same (75.4 °C) as **1** under comparable condition.

Fig. 2 shows the variation of CD and UV spectra with reaction time in *n*-hexane [9] in the polymerization of **1** at 60 °C. The molecular ellipticity (θ) in a 202 nm π–π absorption band due to the amide pairs increases with decreasing UV absorption intensity. Such a hypochromism, i.e. the reverse correlation between the intensities of the ellipticity and UV absorption strongly suggests the generation of an exiton band and a formation of helical conformation of polymer **1** as is well known in polypeptide [10] and DNA [11]. In addition, an enhancement of the θ value with increasing reaction time [12], i.e. decreasing monomer concentration, can be recognized as denoting the increased stereoregulation as the condition is approached to T_c while polymerization proceeds. That is, T_c is gradually

lowered as polymerization progresses since T_c is known to be lowered with decreasing monomer concentration as given by $T_c = (-\Delta G^0 R^{-1})\ln[\text{monomer}]$ [7], in which ΔG^0 denotes the standard free energy and takes a negative value.

CD spectra of the optically active polymer **1** obtained at 30, 50, 60, and 65 °C as well as polymer **2** obtained at 60 °C are shown in Fig. 3. The spectrum pattern of polymer **1** obtained at 60 and 65 °C is different from that obtained at 30 °C, and a small positive cotton effect at 220 nm disappears. While, a strong positive cotton effect at 202 nm appears with increasing polymerization temperature, which is compatible with the decrease of the negative value of $[\alpha]_D$ at higher temperature in Table 1. A bimodal spectrum probably due to a coexistence of helical and non-helical structures with appropriate chain length is observed in the polymer obtained at 50 °C. These are suggestive of two propagating radical species, i.e. helical and non-helical chains. It is noted that the CD intensity of polymer **1** at the largest θ value is very strong, i.e. $[\theta] = \sim 2.7 \times 10^4$ in Fig. 3
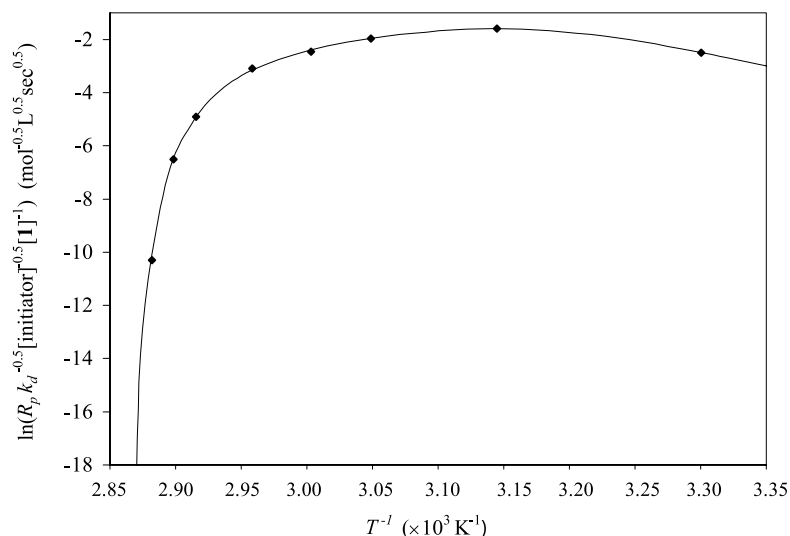

Fig. 1. Graphical determination of ceiling temperature for the polymerization of **1** in benzene and $[\mathbf{1}] = 2.0$ mol L^{-1}.
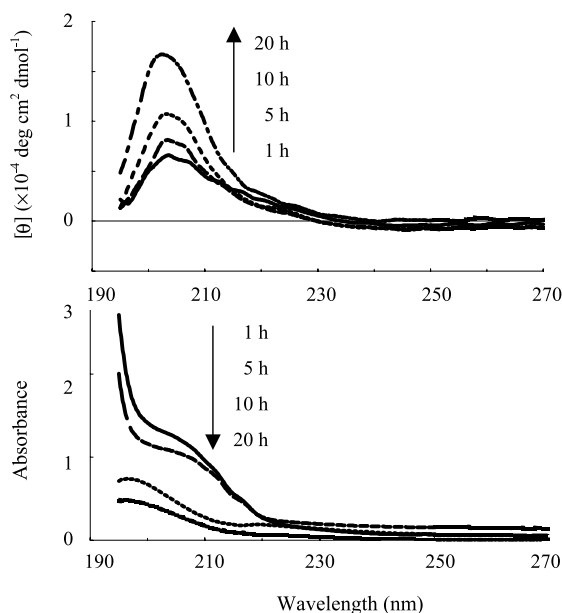
Fig. 2. Dependence of CD and UV spectra of polymer **1** on polymerization time for the polymerization of **1** in benzene and [**1**]=2.0 mol L^{-1} at 60 °C. Spectra were measured in *n*-hexane at 20 °C.

and $[\theta]=\sim 3.9\times 10^4$ [13] for polymer **1** obtained at 55 °C, i.e. in the condition of very close to $T_c=58.5$ °C, in [**1**]= 1.0 mol L^{-1} compared with $[\theta]=\sim 5.0\times 10^3$ for radically-polymerized highly isotactic helical poly(*N*-triphenyl-methylmethacryamide) [14] and is as high as $[\theta]=2.9$– 7.5×10^4 for polypeptides [15]. In ^{1}H NMR spectrum, polymer **1** which was obtained at 60 °C and subsequently hydrolyzed showed two peaks corresponding to unequivalent methylenic protons on the main chain at 2.17 and 2.38 ppm, suggesting an isotactic structure of the polymer because of unequivalent two peaks and equivalent one peak for isotactic and heterotactic polymers, respectively [14,16], although detailed analysis should be necessary [17]. In addition, hydrolyzed polymer **1** still exhibited a CD

spectrum with cotton effect at 198 nm though opposite in sign to unhydrolyzed original polymer **1** [18], indicating an induction of the chiral center in the polymer back born. Situation is similar to polymer **2**, but its CD sign is just opposite to that of polymer **1** as seen in Fig. 3, suggesting polymers **1** and **2** are enantiomers of each other [19].

Fig. 4 shows a variation of CD and UV spectra of polymer **1** which was obtained in the polymerization at 60 °C with measuring temperature in *n*-heptane. CD intensity decreases with increasing temperature as seen in Fig. 4, but it reverts to its original position by reducing temperature, which is in contrast to a random coil polymer **1** which showed no any CD spectral change. Such a reversible CD variation should be due to a change of pitch length of helix, demonstrating a helical structure of polymer **1** which was obtained in the polymerization at 60 °C. Interestingly, the helical structure of polymer **1** was maintained intact even heating at 120 °C for 1 h in anisole according to the CD spectrum. This is probably due to a strong hydrogen bonding between side-chain amide moieties [17] or stiff tertiary and quaternary structure of polymer **1** as compared with conventional polypeptides with main-chain amides [20]. At higher heating, i.e. at 150 °C in anisole for 1 h, random coil polymer **1** was stable, but helical polymer **1** decomposed to a monomer, according to the CD and NMR spectra, probably due to a sterically hindered isotactic helical structure.

The results obtained in the present study are summarized in Fig. 5, where the propagating chain takes preferentially a helical conformation rather than the non-helix including random coil with elevating polymerization temperature or decreasing monomer concentration, i.e. upon approaching the T_c condition. In around T_c, propagation process is at equilibrium (ΔG^0=ca. 0), and thermodynamically stable growing species, helical conformation species in this case, becomes predominant in preference to the kinetically favorable species, i.e. random coil. To the best of our
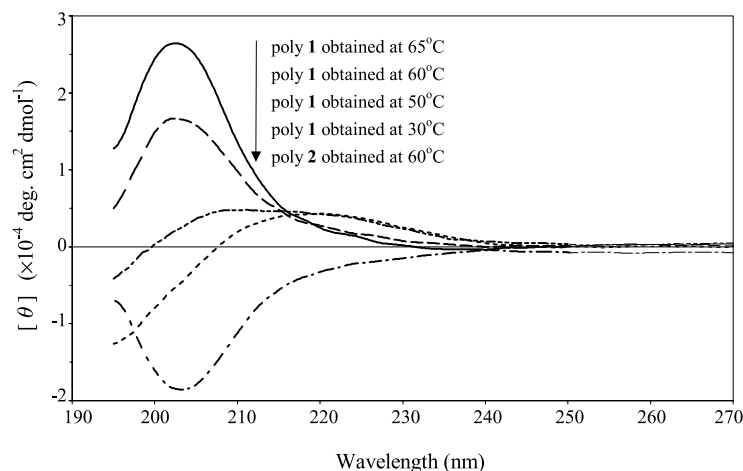

Fig. 3. Variation of CD spectra of polymers **1** and **2** with polymerization temperature for the polymerizations of **1** and **2** in benzene and [monomer]= 2.0 mol L^{-1}. Spectra were measured in *n*-hexane at 20 °C.
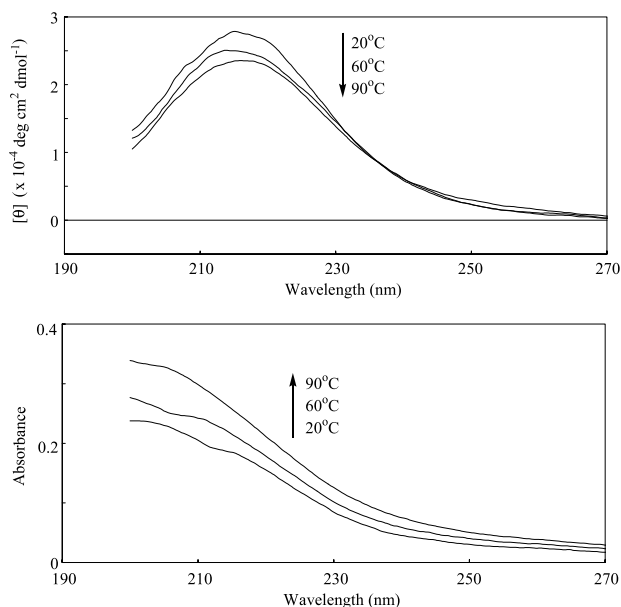
Fig. 4. Variation of CD and UV spectra of polymer **1** which was obtained in the polymerization in benzene and [**1**] = 2.0 mol L^{-1} at 60 °C with measuring temperature in *n*-heptane.

knowledge, there is no report regarding T_c as a controlling condition in the stereostructure and chirality of a polymer, although the dependence of temperature [21] and monomer concentration [22] on tacticity of polymer and the competition between kinetic and thermodynamic controls [22,23] have been known in radical vinyl polymerization and cyclopolymerization.

4. Conclusion

A chiral one-handed heat-resistant helical polymer was synthesized through a conventional radical vinyl polymerization, and it is noted that T_c plays an important role in the stereoregulation and formation of helical structure. The present report suggests that the formation of a helical conformation can be controlled not only by temperature and monomer concentration but also by solvent and pressure.
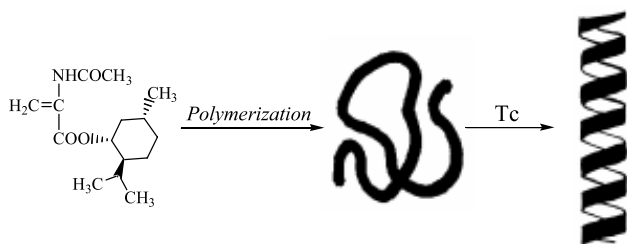

Fig. 5. Change of polymer chain conformation from random coil to helix upon approaching the T_c condition for the polymerization of **1**.

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[12] The negative value of [α]$_D$ was also reduced from −81.2° for monomer to −75.0, −60.8, and −48.0° for the polymers obtained in 2.4, 11.5, and 40.1% conversions, respectively in the same conditions as Fig. 2.
[13] This polymer was obtained in 2.2% yield by the polymerization of **1** with AIBN for 5 h at 55 °C in benzene and [**1**] = 1.0 mol L^{-1}, which gave [α]$_D$ value of −12.1° in CHCl$_3$.
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[17] Absorption due to a trans-hydrogen bonding between neighboring amido groups of polymer side chain in IR spectrum, which can be assigned to an isotactic structure, appeared at 3292 cm^{-1} in the helical polymer **1** in contrast to the random coil polymer **1**. We are now studying about a tacticity of polymer in details.
[18] Because hydrolyzed polymer **1** is insoluble in organic solvents, the CD spectrum in solution cannot be measured, but the spectrum was obtained for the polymer randomly dispersed in Nujol.
[19] Polymerizations of **1** and **2** are identical kinetically because of the same T_c, which also supports an enantiomeric correlation of polymers **1** and **2**.
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