

Synthesis of Chiral Polymer by Mukaiyama Aldol Polymerization and its Characterization

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ABSTRACT

In this paper we have reported the synthesis of chiral polymer by asymmetric aldol polymerization of bis(silyl enol ether) and dialdehyde by Mukaiyama aldol reaction which is one of the most important aldol reaction for chiral polymer synthesis. We have studied the polymerization reaction in two different catalytic conditions such as by using a chiral catalyst viz. 1,1'-binaphthyl-2,2'-diol (BINOL) which is modified by reacting it with diethyl zinc solution in hexane. Another catalyst used for the polymerization reaction is lipase, which is a triacylglycerol hydro lases; EC 3.1.1.3, belongs to a most popular group of enzyme and are used for chiral synthesis. A comparative study has also been made for the polymerization reaction in both the catalytic systems. The results obtained in various reaction conditions by changing amount of catalyst, monomer ratio etc. has also been discussed. The polymers were characterized by IR, NMR, GPC, TGA-DTA, specific rotation and circular dichroism study and it was found that both catalytic conditions give the chiral polymer of approximately same enantioselectivity.

KEYWORDS: *Mukaiyama aldol reaction, BINOL, lipase, circular dichroism*

INTRODUCTION

Asymmetric polymerization is an efficient method to produce optically active polymers from prochiral monomers^[1]. Some of these reactions are successfully utilized as a polymerization reaction to synthesize chiral

polymers. Asymmetric C-C bond forming reaction would be one of the most important types of reaction, which can be applied to asymmetric polymerization. A number of asymmetric C-C bond forming reactions have been developed^[2], some of which can be utilized for the synthesis of optically active polymers.

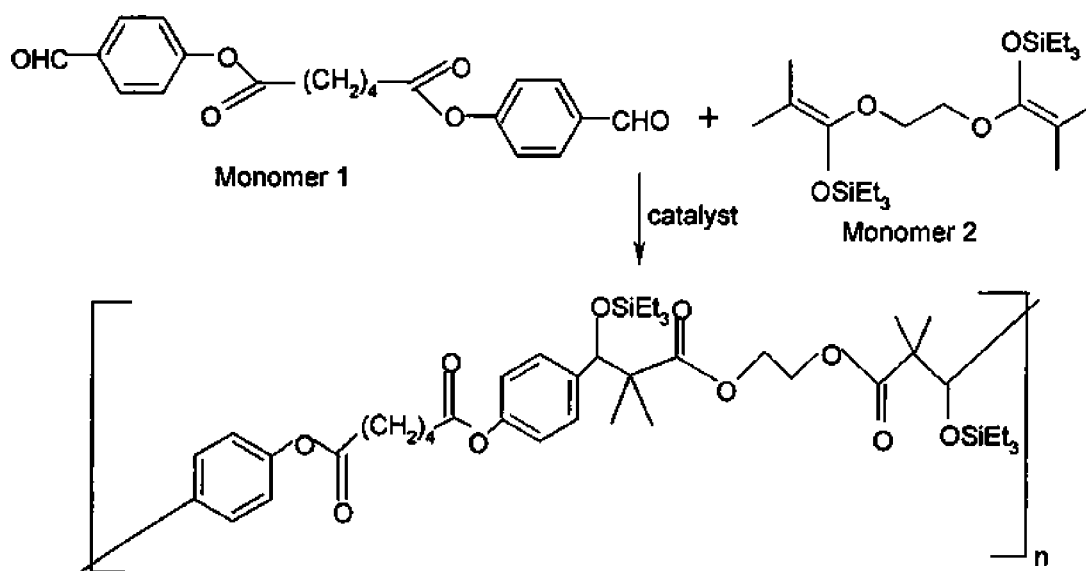
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Nevertheless, asymmetric polymerizations involving this approach have not been studied extensively. Recently, different methodologies have been developed to obtain chiral polymers by asymmetric synthesis^[3]. Among these, Mukaiyama aldol reaction is one of the most important polymerization reactions in which silyl enol ether or silyl ketene acetals react

with aldehyde or ketones to give especially valuable transformations which provide efficient access to β -hydroxycarbonyl derivatives^[4-5]. Asymmetric aldol polymerization of dialdehyde and bis(silyl thioketene acetal) has been successfully demonstrated to yield optically active poly(β -hydroxythioesters)^[6].



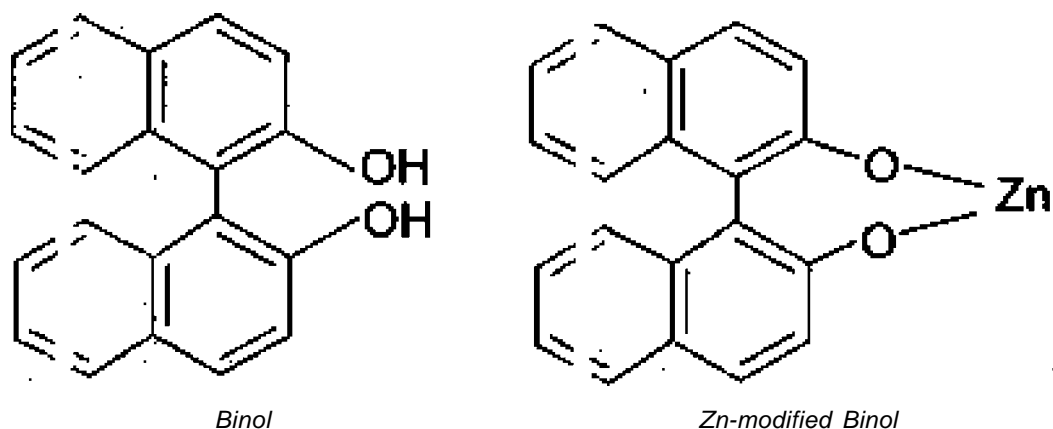
Scheme 1

In this paper we have reported the synthesis of chiral polymer by asymmetric aldol polymerization of bis(silyl enol ether) and dialdehyde by Mukaiyama aldol reaction as shown in Scheme 1 which is one of the most important aldol reactions for chiral polymer synthesis. We have studied the polymerization reaction in two different catalytic conditions by using lipase and modified chiral catalyst. A comparative study has also been made for the

polymerization reaction in both catalytic conditions. This polymerization reaction was studied by Itsuno *et al.*^[3] using $\text{Yb}(\text{Otf})_3$ as chiral catalyst and obtained a polymer of molecular weight 13514.

EXPERIMENTAL

The lipase from *Candida rugosa* (with specific activity 54 units/mg) and BINOL (scheme 1) were procured from Sigma chemicals, USA. Triethylsilane, Ethylene glycol



Scheme 1

dimethacrylate (EGDA), Adipoyl chloride, 4-hydroxy-benzaldehyde, Sodium hydride and the solvents were procured from Ranbaxy Fine Chemical Ltd. New Delhi, India.

IR spectra were obtained on Perkin Elmer, System 2000 FT/IR Infrared spectrophotometer. Data for ^1H NMR and ^{13}C NMR spectra were recorded using BRUKER

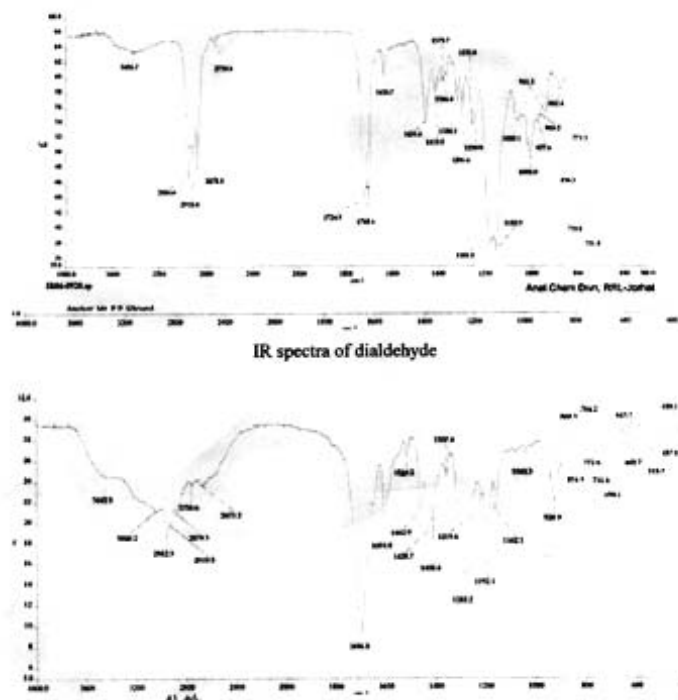


Fig. 1. IR spectrum of 1,2-bis (2-methyl-1-triethylsiloxy-1-propenyloxy)ethane

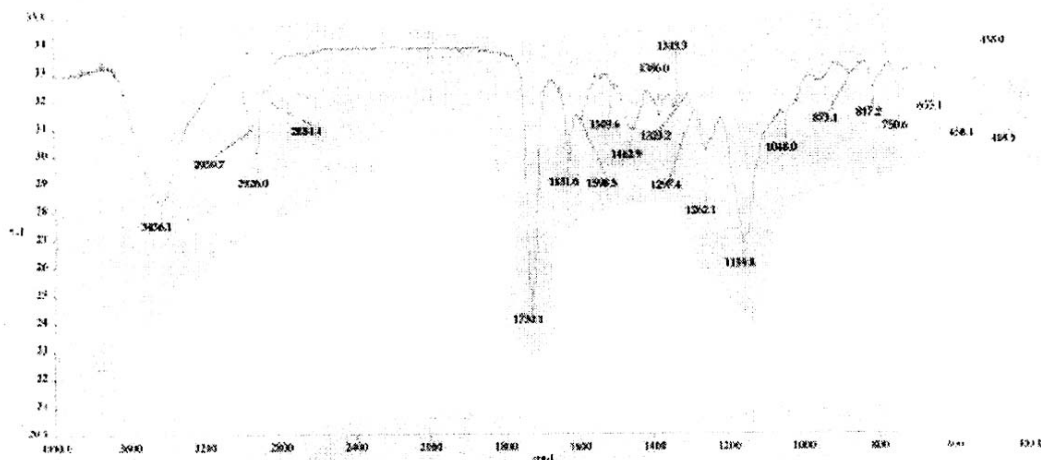


Fig. 2. IR spectrum of polymer

ADVANCE DPX-300 MHz spectrometer. Chemical shifts were reported in ppm down field from tetramethylsilane with solvent resonance as the internal standard. Optical rotations were determined by JASCO Digital Polarimeter P-1020 using chloroform as the solvent. Circular dichroism study was done by JASCO J810C instrument using chloroform as the solvent at a speed 20 nm/min and wavelength range 240-550 nm. The cell path length was 1 cm with a bandwidth 1 nm at a temperature 20°C.

Molecular weight of the polymers were determined by measuring percentage of Silicon in the polymer assuming that copolymer formed in the polymerization reaction was of the type $(AB)_n$ and given in Table 1. Percentage of Silicon in the polymer was measured by X-ray Fluorescence analysis (XRF) on a SPECTRO XEPOS Benchtop XRF Spectrometer (version 1.0).

Thermogravimetry (T_g) and differential thermogravimetry (DT_g) were performed using a Shimadzu Thermal Analyzer 30 at a heating rate of 10°C/min using 5±1 mg of powdered samples in the temperature range from 30°C to 500°C. Differential scanning calorimetry (DSC) was performed on a Perkin Elmer PC series DSC 7 with 3-5 mg of polymer samples weighed in

aluminium pans at a heating rate of 10°C min⁻¹. All experiments were carried out in a nitrogen atmosphere and the measurement was started as soon as the heat flow in the DSC cell had stabilized.

SYNTHESIS OF MONOMER³

Synthesis of Dialdehydet

To a stirred suspension of NaH (0.2 g 8.33 mmol) in anhydrous THF, 1.02 g (8.33 mmol) of 4-hydroxybenzaldehyde was added under N₂ atmosphere, and the mixture was stirred at 0°C for 1 hr. 2.7 mL (24.5 mmol) of Adipoyl chloride was then added and the reaction mixture was stirred for 20 h. After the reaction was completed, a separating funnel separated the aqueous from organic layer. The residual aqueous layer was extracted twice with ethyl acetate. The combined organic layer was dried over Na₂SO₄. The mixture was then filtered and concentrated in a rota vapor to give the solid product and recrystallized the crude product from hexane/EtOAc (yield 22.45%). ¹H NMR (δ in ppm from TMS in CDCl₃): 1.90(br s, 4H), 2.67 (br s, 4H), 7.28 (d, 4H), 7.93 (d, 4H), 10.00 (s, 2H) ¹³C NMR: 24.06, 33.89, 122.26, 131.16, 134.02, 155.29, 170.91, 190.78, mp 97-98; IR(KBr, cm⁻¹) 2951, 2857, 1756, 1698, 1596, 1374, 1261, 1153, 1008, 922, 857, 508. (Fig.3).

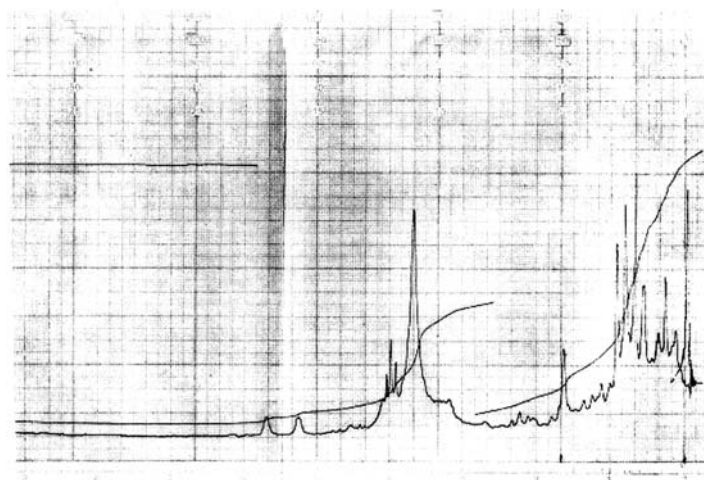


Fig. 3. NMR spectrum of dialdehyde

Synthesis of 1,2-bis (2-methyl-1-triethylsiloxy-1-propenyloxy)ethane(Monomer 2)

2 g (10.4 mmol) of ethylene glyco dimethacrylate and 2.9 g (24.9 mmol) of triethylsilane was mixed with 200 mg of Wilkinson catalyst ($\text{Rh}(\text{PPh}_3)_3\text{Cl}$) and heated to

60°C and stirred for 10 minutes. After fractional distillation under reduced pressure Monomer 2 was obtained as a colorless oil (yield ~ 80%). ^1H NMR (δ in ppm from, TMS in CDCl_3): 0.73 (q, 12H), 0.99 (t, 18H), 1.54 (s, 6H), 1.58 (s, 6H), 3.87 (s, 4H); ^{13}C NMR: 4.9, 6.6, 16.4, 16.9, 67.5, 1.7, 148.4 (Fig. 4).

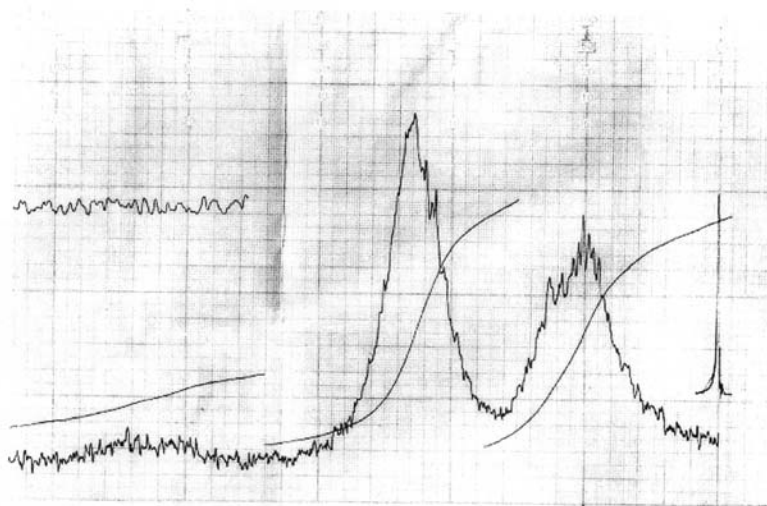


Fig. 4. NMR spectrum of 1,2-bis(2-methyl 1-triethylsiloxy-1-propenyloxy)ethane

SYNTHESIS OF POLYMER

BINOL catalyzed polymerization reaction

Catalytic amount of Binol (as given in Table 1) in dry CH_2Cl_2 was mixed with 1.0 M (0.74 mmol) Et_2Zn hexane solution at room temperature under N_2 . After stirring for 30 min. at ambient temperature, the solvent was removed and the resulting white solid was suspended in 10 ml CH_2Cl_2 and cooled to -5°C . Then a CH_2Cl_2 solution

of monomer 1 and monomer 2 was added successively. The resulting mixture was stirred for 70 hours at ambient temperature. After removal of the solvent, the THF solution of the crude product was poured into $\text{MeOH}/\text{H}_2\text{O}$ (2:1) containing a small amount of aq. HCl. The precipitated polymer was filtered and dried *in vacuo*. This is the general procedure for synthesis of BINOL catalyzed polymer ($\text{P}_1, \text{P}_3, \text{P}_5, \text{P}_7, \text{P}_9$ as given in Table 1) NMR spectrum is shown in Fig. 5.

TABLE 1. Binol and Lipase Catalyzed Polymerization of 1,2-Bis(2-methyl-triethylsiloxy-1-propenyloxy)ethane (M_1) and Dialdehyde (M_2)

Polymer	Amount of monomer 1 (M_1) (mmol/L)	Amount of monomer 2 (M_2) (mmol/L)	Catalyst		Silicon in the polymer (%)	Molecular weight of polymer
			BINOL (mol/L)	Lipase (mg/ml)		
P_1	0.802	0.726	0.428	-	20.72	98100
P_2	0.802	0.726	-	10	20.40	96600
P_3	0.484	0.145	0.428	-	9.47	68300
P_4	0.484	0.145	-	10	9.50	61900
P_5	0.323	0.142	0.428	-	8.70	61700
P_6	0.323	0.142	-	10	7.89	58700
P_7	0.254	0.219	0.428	-	5.25	58200
P_8	0.254	0.219	-	10	4.99	59500
P_9	0.162	0.145	0.428	-	3.89	53600
P_{10}	0.162	0.145	-	10	3.99	53900

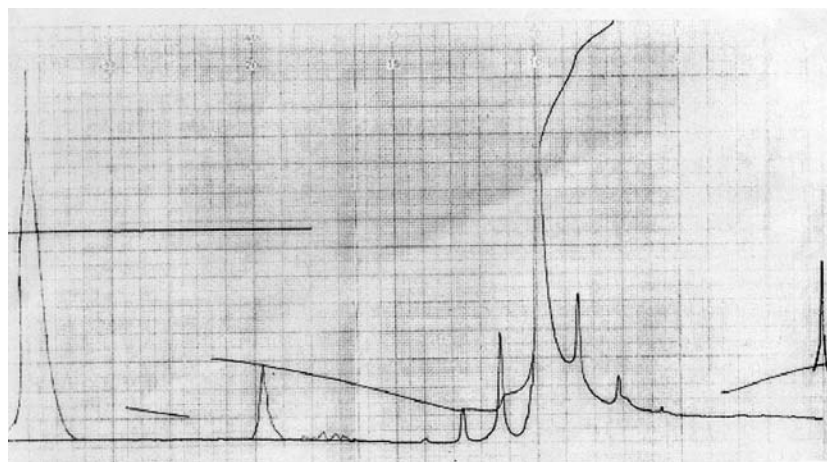


Fig. 5. NMR spectrum of polymer

LIPASE catalyzed polymerization reaction

For lipase catalyzed reaction, catalytic amount of lipase from *Candida rugosa* (as given in Table 1) was added to a toluene solution of monomer 1 and monomer 2 and stirred the reaction mixture for 70 hours at ambient temperature. After removal of the solvent aqueous solution of the mixture was poured into MeOH/H₂O (2:1) solution and dried *in vacuo*. This is the general procedure for synthesis of lipase catalyzed polymer (P₂, P₄, P₆, P₈, P₁₀ as given in Table 1).

RESULTS AND DISCUSSION**Optical properties of the polymer**

Although the determination of optical purity of chiral polymers is definitely very important, many reports on the asymmetric polymerization have not dealt with this point due to its difficulty^[7]. Only a few papers examined to determine optical purity of chiral polymers synthesized by asymmetric polymerization^[8]. However, it is important to investigate the optical purity of chiral polymers. Chromatographic

method is widely used for various kinds of chiral polymers to determine their optical purities. Optical rotation and circular dichroism study also gives an indication of optically pure compound. Optical rotation arises from the differences in refractive index exhibited by the two chiral forms of a molecule, and results in a rotation of the plane of incident linearly polarized light when it passes through a sample of the molecule. Circular dichroism arises as a result of the differential absorption of left and right circularly polarized light by chiral compounds. Such differential absorption at a chiral center arises because of a preferential interaction of the electrons in one optical isomer with the circularly polarized fields of the monitoring light in either the left or right circularly polarized states. The CD signal of each pair of enantiomers is of opposite sign and so the amplitude of a measurement is not proportional to concentration where the mixture of enantiomeric excess; rather it provides an indication of enantiomeric excess. We have

TABLE 2. Optical Properties of Chiral Polymer

Polymer	Optical rotation (in CHCl ₃)	Circular dichroism		
		UV Absorbance	CD Maxima	CD Minima
P ₁	+ 9.2	250 - 2.00	330	245.5
P ₂	+11.8	270 - 2.0	289	255
P ₃	+ 10.2	277 -2.25	318	258
P ₄	+ 9.8	245 - 0.563	307	256
P ₅	- 3.8	245.5 - 0.853	289	255.3
P ₆	+3.2	294 - 0.89	281.5	258
P ₇	+ 3.2	273.5 - 2.26	278	250
P ₈	- 2.6	245 - 2.1	330	251.5
P ₉	+ 3.8	270 - 1.3	280	255
P ₁₀	-13.2	271 - 2.2	281	257.6

studied the optical rotation, CD spectra of the polymer and data are shown in Table 2. Typical CD spectra of chiral polymer catalysed by binol and lipase are shown in Fig. 6.

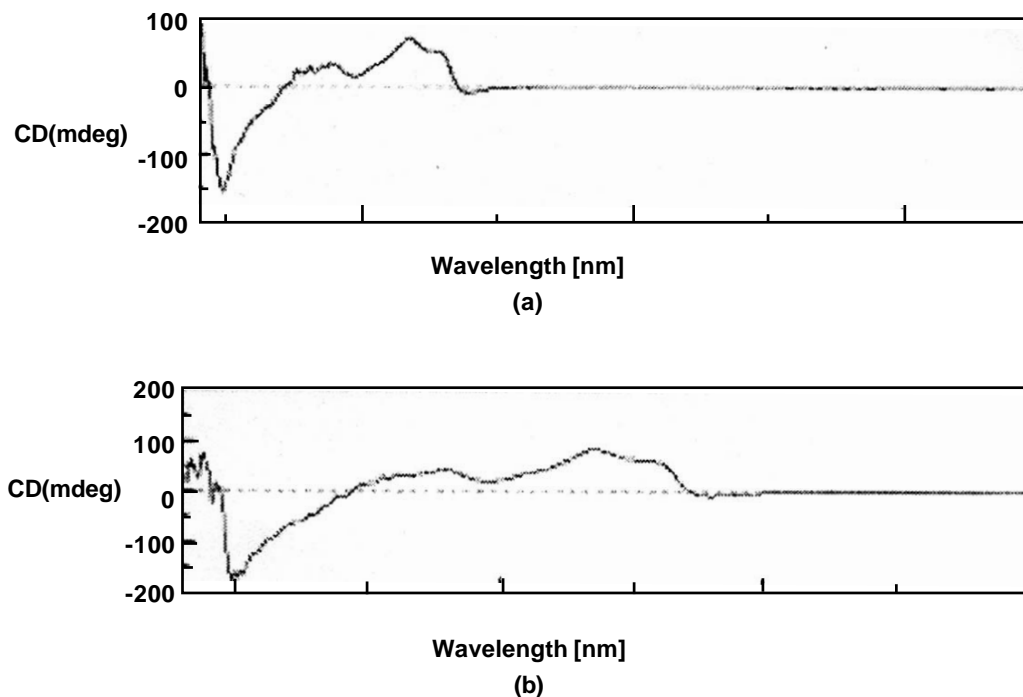
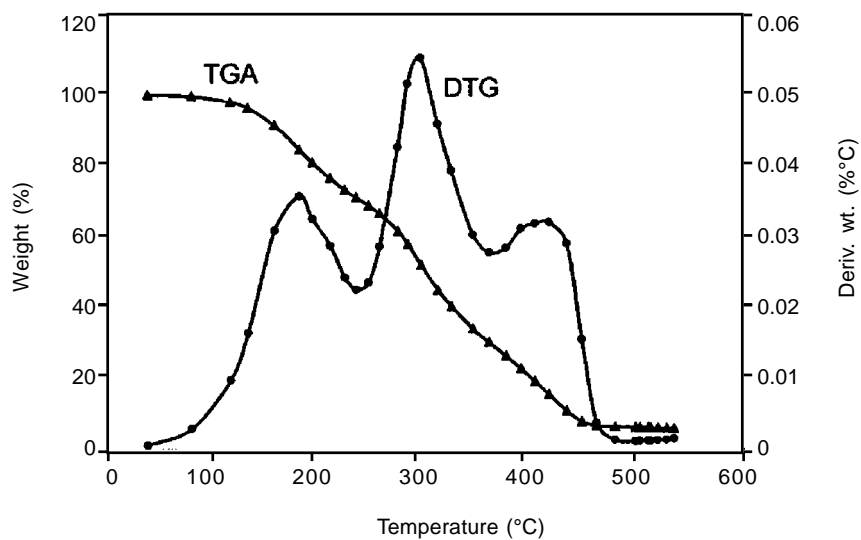


Fig. 6. CD spectra for chiral polymer (a) binol catalyzed (b) lipase catalyzed

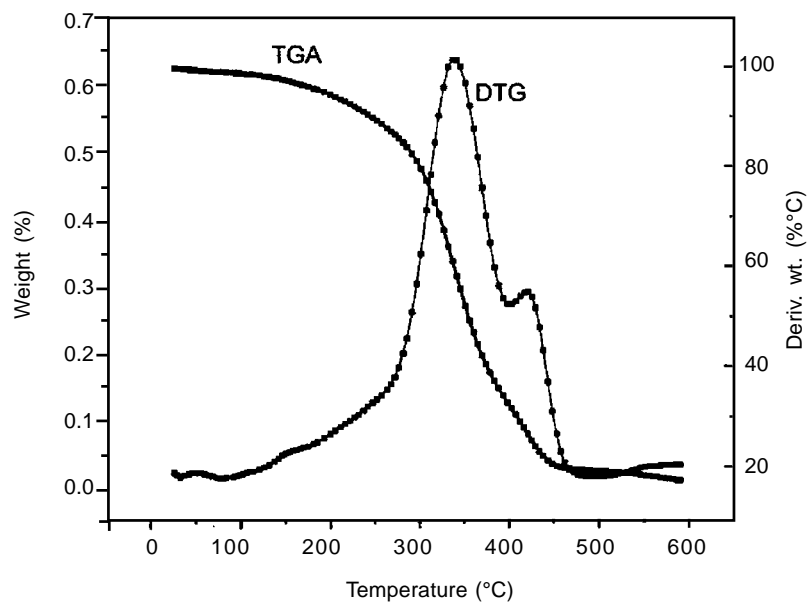
Thermal Properties of Chiral Polymer

The stability of the chiral polymers against thermal stress is of great importance during their use. Hence, thermogravimetric analysis was carried out under the nitrogen atmosphere at a heating rate of 10°C/min.. Typical decomposition curve of the chiral polymer is shown in Fig. 7. The TGA study on the chiral polymer under nitrogen supports apparent two-step decomposition. The first step decomposition starts above 160°C and the second step decomposition start above 280°C.

This corresponds to the random scission of the polymer chain. As the decomposition temperature is high enough, it can tolerate the applied thermal stress during the usage. Furthermore, when the chiral polymer degrades, it leaves nearly no residue at and above 450°C. To make an accurate quantitative prediction on thermal degradation of polymers, the information of the underlying chemical mechanism is insufficient^[9]. Therefore, the development of a molecular level understanding of the thermal degradation of chiral polymers is an important area of research.



(a)



(b)

Fig. 7. Thermogravimetric and differential thermogravimetric curve of chiral polymer
(a) binol catalyzed (b) lipase catalyzed

DSC measurements of the polymer were carried out at a heating rate of $10^{\circ}\text{C min}^{-1}$ in a nitrogen atmosphere. Melting endothermic peak was obtained at 70°C - 260°C for the chiral polymer obtained from Binol catalyzed reaction. Same was obtained at 150°C - 253°C for the chiral polymer obtained from lipase catalyzed reaction. The typical DSC curves of the chiral polymer for both are shown in Fig. 8. The melting point and the heat capacity of the

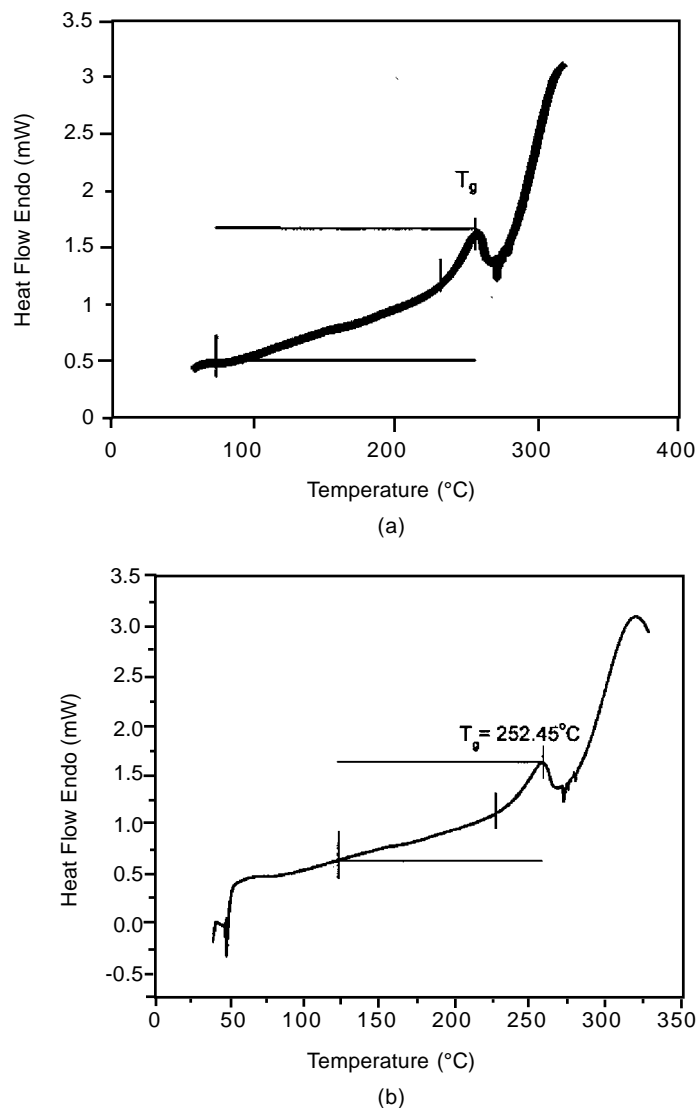


Fig. 8. DSC thermogram of chiral polymer (a) binol catalyzed (b) lipase catalyzed

polymer was determined from the endothermic peaks and was found to be 260°C and 1.2 J/g°C and 252°C and 0.954 J/g* °C respectively for the chiral polymer obtained from binol and lipase catalyzed reactions. The chiral polymer exhibits a single peak indicating the formation of the polymer.

The Mukaiyama aldol reaction requires silyl enol ether or silyl ketene acetal as a substrate, which is usually in a number of cases only prepared in situ and serves as a starting material for aldol products. We synthesized and isolated the bis(triethylsilyl enol ether) as stable and fully characterizable compounds which can be stored for several weeks at -20°C. Since monomers of polyaddition reaction always requires their high purity in order to obtain high molecular weight of polymers, so we attempted to successfully purify the monomers for polymerization reaction.

Lipase catalyzed reactions were carried out at room temperature using toluene as the solvent varying the amount of lipase and amount of monomer. Toluene is the preferred solvent as it gives the enhanced propagation rate and afforded polymers of higher molecular weight^[10]. The lipase concentrations for the reactions were taken from 10 mg/ml to 40 mg/ml, keeping monomer concentration same as that for binol catalyzed reactions. The results showed that with increasing the lipase concentration there are increased rate of monomer consumption. A linear relationship between molecular weight of the polymer and monomer conversions were observed in all enzyme catalyzed reactions. Thus the molecular weight of the polymer can be

controlled by stoichiometry of the reactants for these systems. On the other hand, monomer conversion level as well as molecular weight decreased with increasing enzyme concentration. The amount of monomer consumed in the initiation step can be determined by studying polymerization mechanism, which is our further work of this study.

Binol catalyzed polymerization reactions were carried out at ambient temperature using dichloromethane as the solvent varying the amount catalyst and monomer. In each reaction, binol was modified by treating it with diethyl zinc, as if a chirally modified Lewis acid is used as the polymerization catalyst, each step of the repeated allylation reaction proceeds in asymmetric manner, and an optically active polymer can be easily obtained by asymmetric allylation polymerization. Since asymmetric allylation is a valuable means of constructing chiral functionalized structures, a number of chiral allylmetal reagents directed towards a high level of asymmetric induction have been rationally designed and synthesized^[11]. This result of aldol polymerization encouraged us to carry out the synthesis of optically active polymers by using a chirally modified Lewis acid catalyst. The results of the experiments carried out using chirally modified catalyst and lipase are shown in Table 2. Raise of the temperature in the experiment is the cause to obtain the chiral polymer in low yield accompanied with partial decomposition of the catalyst. From Table 2, it is seen that when monomer concentration increases the molecular weight of the polymer creases for both lipase and Binol catalyzed

reaction for a definite time. But, when binol as well as lipase concentration decreases, keeping monomer concentration constant the molecular weight of the polymer decreases which is due to the lower propagation rate of the polymer. But there are no drastic change of molecular weight in binol and lipase catalyzed reaction. Thus, we can use a stereo selective lipase as polymerization catalyst instead of chiral catalyst. However, the solvent plays an important role for lipase catalyzed reactions as solvents with Log P value from 1.9 to 4.5 showed enhanced propagation rates and afforded polymers of higher molecular weight^[10].

CONCLUSION

We have studied a novel polymerization reaction between bis(triethylsilyl enol ether) and dialdehyde based on Mukaiyama Aldol reaction. The reaction was studied by using chiral catalyst binol and lipase. Both the catalyst efficiently catalyzed the polymerization reaction.

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