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Anionic Alternating Copolymerization of Ketene and Aldehyde: Control of Enantioselectivity by Bisoxazoline-Type Ligand for Synthesis of Optically Active Polyesters

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Tremendous effort has been devoted to the development of enantioselective polymerization. In these studies, syntheses of optically active polymers by enantioselective polymerization of achiral monomers have been attempted, and the excellent results have been reported.[1]

In this communication, we report a new enantioselective copolymerization system based on the alternating copolymerization of ketene and aldehyde. Anionic alternating copolymerization of ketenes and aldehydes affords the corresponding polyesters,[2] and we have developed the living anionic alternating copolymerization of ethylphenylketene and aromatic aldehydes.[3] This copolymerization system is an attractive target for stereocontrol because the resultant polyesters have two adjacent chiral centers in the repeating unit. In our recent study, we found that the diastereoselectivity between the two chiral centers can be controlled by choosing appropriate solvents and additives.[4] Diastereoselectivity of the repeating unit remarkably affected the physical properties of the polymers such as solubility, thermal property, and density. In this study, the highly enantioselective copolymerization was accomplished using zinc as the countercation and optically active bis(oxazoiline) ligand.

We recently reported an attempt to control the enantioselectivity in the copolymerization of ethylphenylketene and benzaldehyde using diethylzinc (Et_2Zn) as the initiator in the presence of optically active bis(oxazoline) ligand, (*S*,*S*)-(−)-2,2′-isopropylidenebis(4-*tert*-butyl-2-oxazoline) (^{t}Bubox).[5] In this copolymerization, Et_2Zn did not initiate the polymerization, but it was activated through bidentate coordination with ^{t}Bubox to initiate the polymerization, affording the corresponding polymers quantitatively. Such activation of Et_2Zn by coordination with the ligands is widely utilized in asymmetric organic syntheses.[6] These features imply that polymerization with no coordination, which cannot control enantioselectivity, does not proceed. Therefore, a design of appropriate ligands may enable us to control the enantioselectivity in the copolymerization of ethylphenylketene and benzaldehyde. However, this copolymerization system using the bidentate coordinating ^{t}Bubox did not provide an optically active polymer under a variety of conditions.[5] Because the bidentate ^{t}Bubox would be insufficient to fill the vacant orbitals of the zinc, we next chose tridentate (*S*,*S*)-(−)-2,6-bis(4-isopropyl-2-oxazolin-2-yl)pyridine (Pybox, Scheme 1).[7]

Scheme 1. Copolymerization of Ethylphenylketene and Benzaldehyde in the Presence of Optically Active Ligands

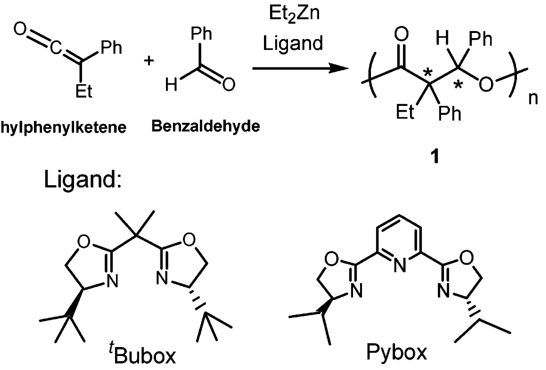

Table 1 summarizes the results of the polymerization in the presence of Pybox. When the Et_2Zn−Pybox complex (1:1.2) was added to a solution of ethylphenylketene and benzaldehyde in THF at −40 °C (entry 1), the characteristic yellow color of ethylphenylketene disappeared within 72 h, indicating the quantitative conversion to form a polymer. The main chain structure of the resulting polymer was confirmed to be polyester by its characteristic IR absorption at 1737 cm^{-1}.[3−5] The obtained polymer showed optical activity {specific optical rotation ($[\alpha]_D^{25}$) = −16°}, indicating that our design of tridentate Pybox is appropriate for stereocontrol. Accordingly, Pybox was selected for the optimization of stereocontrol. Examination of the solvent effect on enantioselectivity revealed that CH_2Cl_2 is the optimal solvent to afford the polymer with $[\alpha]_D^{25}$ of −125° (entries 1−3). The effect of polymerization temperature on the polymerization in CH_2Cl_2 was then evaluated. As shown in entries 3−6, decreasing polymerization temperature increased the specific optical rotation of the polymers, and the highest optical rotation was achieved at −78 °C ($[\alpha]_D^{25}$ = −158°, entry 6).[8,9]

In order to evaluate the stereochemistry of the obtained optically active polymers in detail, the main chain was reductively degraded by treatment with lithium aluminum hydride in refluxing THF (Scheme 2).[10] In all cases, the polyesters could be completely degraded to give the corresponding diols **2**. The diastereomeric ratio (**2a**:**2b**) of the diols was more than 90:10, indicating that the polymerizations proceed with high diastereoselectivity.[11]

Next, determination of optical purity of the isolated **2a** was attempted. Various attempts of chiral high-performance liquid chromatographic (HPLC) analysis involving chemical transformation of **2a** into its derivatives revealed that diacetate **3** can be successfully separated into the enantiomers (Scheme 2).[12] Thus, the enantioselectivity of the copolymers were evaluated by chiral HPLC analysis (Chiralcel OD-H column) of **3**. As shown in Table 1, correlation between enantiomeric excess (% ee) and $[\alpha]_D^{25}$ of the polymers is positive, and the optical purity of **3** derived from the polymer with the highest $[\alpha]_D^{25}$ reached a maximum value of 80% ee (entry 6).

Figure 1 depicts the circular dichroism (CD) and UV spectra of the polymers with different enantioselectivities. The CD peaks of the all polymers appeared at about 235 nm which corresponds to the n → π^* electron transition of carbonyl groups in the ester

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Table 1. Anionic Copolymerization of Ethylphenylketene and Benzaldehyde with Et$_2$Zn in the Presence of Pybox[a]

entry	solvent	temp/°C	yield/%[b]	M_n (M_w/M_n)[c]	**2a**/**2b**[d]	[α]$_D^{25}$ [e] (deg)[f]	%ee[g] of **3**[h]
1	tetrahydrofuran	−40	92	9800 (1.55)	93/7	−16	18
2	toluene	−40	92	26 000 (1.89)	91/9	−58	56
3	CH_2Cl_2	−40	90	20 000 (1.70)	93/7	−125	74
4	CH_2Cl_2	0	92	4700 (1.44)	90/10	−41	38
5	CH_2Cl_2	−20	90	10 400 (1.59)	89/11	−97	62
6	CH_2Cl_2	−78	90	22 700 (2.28)	94/6	−158	80

[a] Polymerization conditions: $[Et_2Zn]_0 = 0.02$ M; $[Pybox]_0/[Et_2Zn]_0 = 1.2$; $[ethylphenylketene]_0/[benzaldehyde]_0/[Et_2Zn]_0 = 15/16/1$. [b] MeOH-insoluble parts. [c] M_n = number-average molecular weight. M_w/M_n = molecular weight distribution. Estimated by size-exclusion chromatographic analysis (eluent: tetrahydrofuran, polystyrene standards) of the crude products. [d] **2a** = *threo*-2-ethyl-2-phenyl-1-phenylpropanediol. **2b** = *erythro*-2-ethyl-2-phenyl-1-phenylpropanediol. Determined by high-performance liquid chromatographic analysis using silica gel column (eluent: Hex−^{i}PrOH(v/v = 95/5)) after reductive degrdation. [e] [α]$_D^{25}$ = specific optical rotation. [f] c = 1 g/dL, $CHCl_3$. [g] %ee = enantiomeric excess. [h] Determined by high-performance liquid chromatographic analysis using Chiralcel OD-H column (eluent: Hex−^{i}PrOH (v/v = 99/1)).

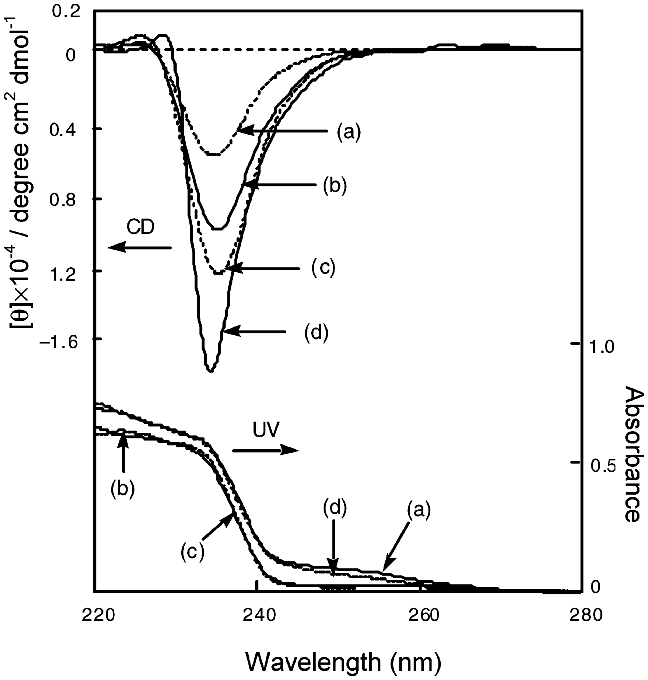
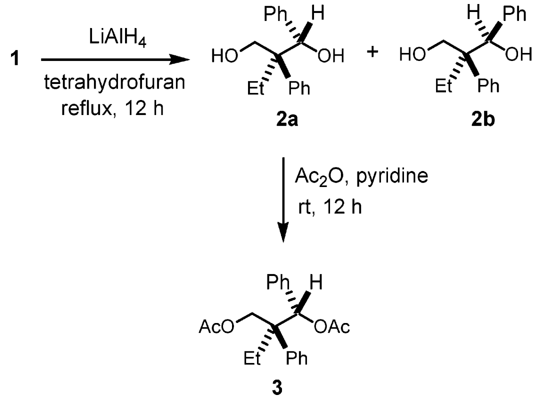


Figure 1. CD and UV spectra of the copolymers (c = 1 g/dL, $CHCl_3$): (a) 38% ee (Table 1, entry 4), (b) 56% ee (entry 2), (c) 74% ee (entry 3), and (d) 80% ee (entry 6).

Scheme 2. Determination of Diastereoselectivity and Enantioselectivity



moiety.[13] This indicates that the polymer main chains may possess highly ordered structures, and the optical rotations of the polymers are ascribed to the enantioselectivity in the main chain induced by the Et_2Zn−Pybox complex. The peak intensity gradually increased with an increase of enantiomeric excess, suggesting that highly ordered structures may be gradually induced as the enantioselectivity in the polymer chain enhances, although it needs further examination.

Further, the optical activity of the polymers has remarkable effects on their solubility and thermal property. The optically not active polymers are less soluble in common organic solvents such as THF, toluene, CH_2Cl_2, and $CHCl_3$, whereas the optically active polymers are soluble in the above solvents. The 5% weight loss temperatures (T_{d5}s) of the polymers increase linearly as the enantiomeric excess increases (see Supporting Information). The thermal resistance can be controlled over a 100 deg temperature ranges (T_{d5} = 220 −320 °C) by the enantioselectivity of the polymer chain.

In summary, we showed the first example of enantioselective anionic alternating copolymerization of ethylphenylketene and benzaldehyde. Pybox proved to be an effective ligand stereocontrol to afford the optically active polyesters with high enantioselectivity. The highly ordered structures of the polymers, induced by the enantioselectivity, improve their solubility and thermal property. Further studies are focused on determining the absolute configuration of the polymer main chain.

Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) Pybox is widely utilized in asymmetric organic syntheses For example, see: (a) Desimoni, G.; Faita, G.; Quadrelli, P. *Chem. Rev.* **2003**, *103*, 3119−3154 and references therein. (b) Nishiyama, H. *Enantiomer* **1999**, *4*, 569−574.

(8) Experimental details are given in the Supporting Information.

(9) Although the effects of amounts of Pybox were changed (Pybox/Et_2Zn = 2.4, 5.0, 10.0), the enantioselectivities did not enhanced.

(10) Experimental details are given in the Supporting Information.

(11) The relative stereochemistry of the polymer main chain has already been assigned; from this, the diol was converted to the cyclic carbonate, and its single crystal was analyzed by X-ray crystallography (see ref 4).

(12) Experimental details are given in the Supporting Information.

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