Stereoselective Polymerization of α-Amino Acid *N*-Carboxyanhydrides with Nickel *dl*-2-Methylbutyrate–Tri-*n*-butylphosphine Catalyst System

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ABSTRACT: Courses of polymerization of *N*-carboxyanhydrides of γ-benzyl L- and DL-glutamate and of L- and DL-alanine with nickel *dl*-2-methylbutyrate-tri-*n*-butylphosphine catalyst system and with *n*-hexylamine were followed by the ir spectroscopic method. These kinetic results revealed clearly the significant difference in behavior observed between nickel catalyst and amine catalyst and suggest that the former has a stereoregulating power higher than the latter or nickel acetate catalyst system. This interpretation was supported by DL copolymerization of γ-benzyl glutamate *N*-carboxyanhydride and the main-chain configuration of its polymer.

Polymerization of α-amino acid *N*-carboxyanhydride (α-amino acid NCA) initiated by an amine or an alkali metal compound is reported to be started with the attack of lone-pair electrons in the catalyst molecule to the C-5 atom in the NCA ring or with the withdrawal of a proton from the NH group in the NCA and to be propagated through a free amino group or an imide anion formed in the initial reaction.[2-5] If these proposed mechanisms are correct, these catalysts should have no highly stereocontrolling power toward DL-α-amino acid NCA and the steric structure of the polymer should be controlled solely by the penultimate effect.[6,7] In fact, regular α-helix content in the polymer prepared by an amine catalyst and rate of polymerization decreased with an increase in the amount of enantiomorphic NCA.[5,8]

The stereoselective polymerizations of γ-benzyl DL-glutamate *N*-carboxyanhydride (DL-BG-NCA) and DL-alanine *N*-carboxyanhydride (DL-Ala-NCA) were studied with a nickel carboxylate–tributylphosphine catalyst system and with an amine catalyst. For these purposes, ir spectroscopic methods were applied for analyzing polymer structures kinetically and structurally.

Nickel acetate-tri-*n*-butylphosphine (*n*-Bu$_3$P) catalyst system, the characteristic behavior of which was reported in a previous paper,[9] is difficult to apply adequately, because the polymerization cannot proceed throughout in a homogeneous state under the condition of Ni–*n*-Bu$_3$P = 1:43 (mol/mol).[9] This difficulty could be overcome by using higher carboxylates, especially those of 2-methylbutyrate. Nickel *dl*-2-methylbutyrate is readily soluble in the usual organic solvents and has an additional merit in having an asymmetric carbon atom. Thus, optically active or inactive (racemic) catalyst systems can be prepared in response to the specific requirement.

In order to know the effect of bulkiness of the side group of monomer on the kinetic analysis of the stereoselective polymerization, the polymerization of DL-NCA with nickel *dl*-2-methylbutyrate-tri-*n*-butylphosphine catalyst system (*dl*-Ni catalyst) was studied using two kinds of NCA, *i.e.*, DL-Ala-NCA has the shortest side group, while DL-BG-NCA has a long and bulky one. To know the stereoregulating capacity of this catalyst system, DL copolymerizations of L- and DL-BG-NCA with the *dl*-Ni catalyst were studied in respect to the structural analysis of the polymer.

Experimental Section

Materials. L- and DL-BG-NCA, prepared by reacting phosgene[9] with γ-benzyl glutamate, were recrystallized five times from chloroform–*n*-hexane and five times from ethyl acetate–*n*-hexane (or *n*-pentane) with our special types of apparatus:[9] L-BG-NCA, yield 80.0%, mp 92–93°, $[\alpha]^{20}\mathrm{D}$ −17.1° (*c* 3.32, ethyl acetate). *Anal.* Calcd for $C_{13}H_{13}NO_5$: C, 59.31; H, 5.05; N, 5.44. Found: C, 59.49; H, 5.05; N, 5.28. DL-BG-NCA, yield 71.4%, mp 86–87°. *Anal.* Found: C, 59.24; H, 4.87; N, 5.44.

L- and DL-alanine *N*-carboxyanhydrides (L- and DL-Ala-NCA) were prepared by the same method as L- and DL-BG-NCA.[10] L-Ala-NCA, mp 92° *Anal.* Calcd for $C_4H_5NO_3$: C, 41.74; H, 4.38; N, 12.17. Found: C, 41.62; H, 4.34; N, 12.24. DL-Ala-NCA, mp 45°. *Anal.* Found: C, 41.68; H, 4.46; N, 12.30.

Nickel *dl*-2-methylbutyrate was prepared by the following method. To a suspension of 18 g (0.05 mol) of $NiCO_3 \cdot 2Ni(OH)_2 \cdot 4H_2O$ in 100 ml of tetrahydrofuran, 10.2 g (0.1 mol) of *dl*-2-methylbutyric acid was added with stirring under an argon atmosphere. The mixture was kept at the refluxing temperature for 48 hr. The filtrate of the green tetrahydrofuran solution was evaporated to dryness *in vacuo*. The residue was purified by reprecipitating five times from the tetrahydrofuran (5 ml)–*n*-hexane (or *n*-pentane, 50 ml) mixture. *Anal.* Calcd for $C_{10}H_{18}NiO_4$: C, 46.03; H, 6.95. Found: C, 45.90; H, 6.44.

n-Hexylamine and benzylamine were dried successively over NaOH pellet and over Na–K alloy, and then distilled under reduced pressure.

Solvents were purified in the same manner as described in a preceding paper.[9]

Polymerization Methods. L- and DL Copolymerization of BG-NCA. A solution of 0.5 g (1.91 mol) of BG-NCA in 10 ml of dioxane was polymerized with Ni catalyst, which was prepared by reacting nickel carboxylate with *n*-Bu$_3$P in 0.5 ml of dioxane at 30° for 75 min, at 30° under an argon atmosphere using our polymerization tube.[9] The polymerization was terminated by adding 200 ml of ethanol. The polymer separated by filtration was dried *in vacuo* at 80° for 48 hr.

Kinetic Measurement. Polymerization reaction was followed by ir spectral analysis in the range of 1900–1500 cm^{-1} using a Jasco Model DS-402 spectrometer in a 0.1-mm KBr liquid cell under an argon atmosphere at 25°. Weak absorption bands due to the solvent (dioxane) were compensated using the reference cell.

Characterization of the Polymer. Intrinsic viscosity of dichloroacetic acid solution of the polymer was measured at 25.0 ± 0.1°. Molecular weight was calculated from the intrinsic viscosity using the equation,[11] $[\eta] = 2.78 \times 10^{-5} \bar{M}_w^{0.87}$.

Specific rotation and ORD were measured using three different polarimeters (Yanagimoto Model ORD-185, Jasco automatic polarimeter Model DIP-SL, and Jasco Model J-20) in dichloroacetic acid and in chloroform solutions at 20.0°. In these measurements, two different 20-mm cells were used for checking the reproducibility of the data.

Ir spectral analysis of the polymer film which was prepared by casting from chloroform solution was measured using a Jasco Model DS-402G spectrometer in the range from 4000 to 400 cm^{-1}. The ir spectral data obtained by converting the transmittance to the optical density were analyzed using a Du Pont 301 curve resolver to determine the peak area of the individual peak.

Results and Discussion

I. Kinetic Analysis of Polymerization of Amino Acid NCA. For the studies on the stereoselectivity of nickel carboxylate-tri-*n*-butylphosphine catalyst system, rates of polymerization of Ala-NCA or BG-NCA were compared in four different polymerization systems: (i) DL-NCA with

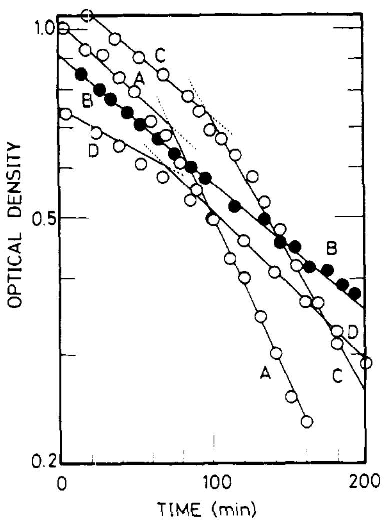

Figure 1. Time dependence of the optical density of the ir band at 1860 cm^{-1} in the polymerization medium: (A) L-BG-NCA-amine, (B) DL-BG-NCA-amine, (C) L-BG-NCA-(Ni-P), and (D) DL-BG-NCA-(Ni-P).

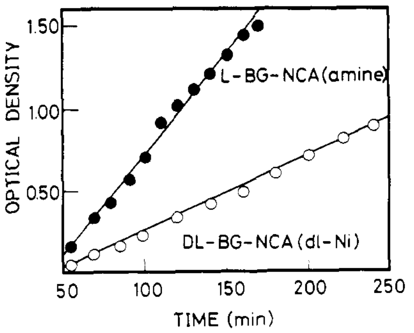

Figure 2. Time dependence of the optical density of the band at 1655 cm^{-1} in the polymerization medium. Solid lines are calculated with eq 5.

the *dl*-Ni catalyst, (ii) DL-NCA with *n*-hexylamine, (iii) L-NCA with the *dl*-Ni catalyst, and (iv) L-NCA with *n*-hexylamine.

A. Polymerization of L- or DL-BG-NCA. L- or DL-BG-NCA and its polymer (P-L- or P-DL-BG) are readily soluble in organic solvents usually used for the polymerization of a NCA, such as tetrahydrofuran, dioxane, and chloroform. The course of polymerization was followed by ir spectroscopy. BG-NCA has characteristic absorption bands at 1860, 1790, and 1735 cm^{-1}, and P-BG has characteristic absorption bands at 1655 (amide I) and 1550 cm^{-1} (amide II), which are related to α-helix conformation.[12]

The rate of polymerization was measured ir spectroscopically by following the intensity change of the absorption band at 1860 cm^{-1} in dioxane solution with the method proposed by Doty *et al.*[13]

1. Polymerization with *n*-Hexylamine. *n*-Hexylamine, which has no absorption band and hardly appears in the range of 1900–1500 cm^{-1}, was added to the 5% dioxane solution of BG-NCA in a molar ratio of NCA–amine of 20, and the optical density of the NCA was measured at every 10-min interval. The time dependence of the amount of L-BG-NCA is represented by two straight lines intersected at about 60 min, in good agreement with the result reported by Idelson and Blout,[13] while that of DL-BG-NCA follows a single straight line up to 200 min (Figure 1).

The rate constants were calculated from these values using eq 1.[13,14]

$$k = \ln (D^1/D^2)/(t_2 - t_1)[I] \qquad (1)$$

where D^1 and D^2 denote optical densities of the band at 1860 cm^{-1} at time t_1 and t_2, and k and [I] denote the rate constant and the concentration of the catalyst (initiator), respectively. The calculated rate constants were, $k_1 = 7.08 \times 10^{-3}$ l./(mol sec), $k_2 = 24.62 \times 10^{-3}$ l./(mol sec) for L monomer and $k = 6.93 \times 10^{-3}$ l./(mol sec) for DL monomer.

In the polymerization of L-BG-NCA, an absorption band assigned to the amide group in α helix (1655 cm^{-1}) began to appear at about 60 min, which corresponded to the intersecting point of the two straight lines representing the monomer consumption, and its optical density increased with time (Figure 2). In the case of DL-BG-NCA, on the other hand, the same band (1655 cm^{-1}) was too complex to be measured accurately, presumably because of the chain conformation of the growing polymer being complex.

The rate of consumption of the NCA [M] may be expressed by

$$-d[M]/dt = k[I][M]$$

or

$$-d[M]/dt = k[M^-][M] \qquad (2)$$

where $[M^-]$ denotes "activated monomer." If the monomer consumed is assumed to be converted exclusively to the polymer, the amount of polymer [P] produced in the time interval between t_1 at which intersecting point begins to appear and t_2 $(t_2 \geq t_1)$ can be represented by

$$\begin{aligned} [P] &= [M_1] - [M_2] \\ &= [M_1]\{1 - \exp(k_2[I](t_1 - t_2))\} \\ &= [M_0]\{\exp(-k_1[I]t_1)\}\{1 - \exp(k_2[I](t_1 - t_2))\} \\ &= [M_0]\{\exp(-k_1t_1[I])\}k_2[I](t_2 - t_1) \qquad (3) \end{aligned}$$

In equations, $[M_0]$, $[M_1]$, and $[M_2]$ denote the concentration of NCA at polymerization time, t_0, t_1, and t_2, respectively. k_1 and k_2 represent the rate constant in the range of $0 \leq t \leq t_1$ and $t_1 \leq t \leq t_2$, respectively.

The optical density at 1655 cm^{-1} was found to obey Lambert–Beer's equation in the form of

$$D_{1655} = \mathrm{const}\,d[P] \qquad (4)$$

where d and [P] denote the cell length and the concentration of the α helix, respectively. Equation 5 was derived by combining eq 3 and 4.

$$D_{1655} = \mathrm{const}\,d[M_0]k_2[I](t_2 - t_1) \exp(-k_1t_1[I]) \qquad (5)$$

Since values of const, d, $[M_0]$, and [I] are known values, k_1, t_1, and k_2 can be calculated with eq 2 using the data shown in Figure 1. These calculated values agree fairly well with the observed values (Figure 2). These results appear to show that, in the polymerization of L-BG-NCA by *n*-hexylamine, most of the NCA consumed in the second fast reaction is converted to the polymer having the α-helix conformation. In contrast, in the polymerization of DL-BG-NCA by *n*-hexylamine, the NCA is converted to form the polymer having complicated conformations. These interpretations are supported by the main-chain conformation assumed by the polymer obtained by the DL copolymerization (see later in this paper).

2. Polymerization with *dl*-Ni Catalyst. The polymerization of L- or DL-BG-NCA with *dl*-Ni catalyst was carried out in the same condition as that with *n*-hexylamine

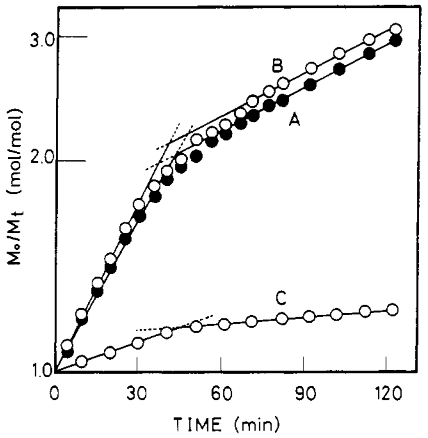

Figure 3. Polymerization of Ala-NCA with the *dl*-Ni catalyst: (A) L-Ala-NCA:n-Bu$_3$P:Ni salt = 2:2:1 (molar ratio), (B) DL-Ala-NCA:n-Bu$_3$P:Ni salt = 2:2:1, (C) DL-Ala-NCA:n-Bu$_3$P:Ni salt = 8:2:1.

catalyst. The *dl*-Ni catalyst was prepared in rigorously defined conditions, because the stereoregularity of the polymer depends on the preparation method, especially on the aging time. The *dl*-Ni catalyst was prepared by reacting the Ni salt with the phosphine in a molar ratio of 1:10 at 30° for 20 min and was used as a catalyst in a molar ratio of the Ni salt to the NCA of 1:8.

The rate of consumption of L-BG-NCA with the *dl*-Ni catalyst is represented by two straight lines intersecting at 100 min, quite similarly to the case of L-BG-NCA by n-hexylamine. In the polymerization of DL-BG-NCA with *dl*-Ni catalyst, the time dependence of the monomer consumption is represented also by two straight lines intersecting at 80 min, in striking contrast with the polymerization of DL-BG-NCA with n-hexylamine. The polymerization rate constants calculated with eq 1 are $k_1 = 7.5 \times 10^{-3}$ l./(mol sec) and $k_2 = 18.3 \times 10^{-3}$ l./(mol sec) for L monomer, and $k_1 = 5.7 \times 10^{-3}$ l./(mol sec) and $k_2 = 9.4 \times 10^{-3}$ l./(mol sec) for DL monomer.

In the polymerization of DL-BG-NCA with *dl*-Ni catalyst, the optical density of the absorption band at 1655 cm^{-1}, which began to appear apparently at about 75 min, increased with time, similarly to the case of the polymerization of L-BG-NCA with n-hexylamine (Figure 2). The calculated optical density agrees well with the observed value. The consumption of DL-BG-NCA is therefore attributable to the formation of the polymer having α-helix conformation.

B. Polymerization of L- or DL-Ala-NCA. Stereoselective polymerization of Ala-NCA was studied in an anisole solution. Polyalanine (P-Ala) is known to be sparingly soluble in ethereal solvents usually used for polymerization of NCA such as dioxane and tetrahydrofuran because of its side chain being shortest among poly(α-amino acids). Although P-Ala is reported to be more soluble in halogenated hydrocarbons, such as chloroform, dichloromethane, and 1,2-dichloroethane than in ethereal solvents,[15] the stereoselective polymerization of DL-Ala-NCA did not proceed to completion in such halogenated solvents. Anisole proved to be the best solvent for the polymerization.

The intensity of α-helix band at 1305 cm^{-1} [16] did not provide a reliable measure of the α-helix content in the polymerization with this catalyst, because it exists in the fingerprint region and is liable to be influenced by the presence of other bands. Therefore, stereoselective polymerization of Ala-NCA with *dl*-Ni catalyst was followed kinetically by the decrease in the intensity of the absorption band at 1850 cm^{-1} which is assigned to C-2 carbonyl group in the NCA ring.

Table I
Copolymerization of γ-Benzyl L- and DL-Glutamate N-Carboxyanhydride with $(dl\text{-}C_2H_5(CH_3)CHCOO)_2Ni$–$n$-Bu$_3$P Catalyst System[a]

	f_L (%)	Yield (%)	$[\alpha]^{20}D$ (deg) (CCl_2H-COOH)	$[\alpha]^{20}D$ (deg) ($CHCl_3$)	Mol Wt[b] (× 10^{-4})
N-1	100	17.0	−17.0	+15.3	14.7
N-2	90	6.8	−16.5	+17.2	6.55
N-3	80	6.2	−15.6	+22.4	1.97
N-4	70	8.7	−10.6	+24.8	2.45
N-5	60	7.6	−7.6	+15.5	3.80
N-6	55	17.9	−3.7	+14.4	2.33
N-7	50	24.6	0	0	6.02

[a] Polymerization under the condition of NCA (1.91 mmol):n-Bu$_3$P:Ni$^+$ = 280:11.8:1 (molar ratio) in 10 ml of dioxane at 30° with aging for 75 min. [b] In dichloroacetic acid at 25°.

Table II
Copolymerization of γ-Benzyl L- and DL-Glutamate N-Carboxyanhydride with Benzylamine[a]

	f_L (%)	Yield (%)	$[\alpha]^{20}D$ (deg) (CCl_2H-COOH)	$[\alpha]^{20}D$ (deg) ($CHCl_3$)	Mol Wt[b] (× 10^{-4})
A-1	100	41.9	−17.0	+16.0	3.34
A-2	90	46.2	−11.9	+24.9	2.50
A-3	80	46.7	−9.5	+33.9	1.99
A-4	70	53.4	−6.8	+38.7	2.06
A-5	60	38.9	−3.8	+34.5	2.38
A-6	55	26.9	−1.4	+18.6	2.96
A-7	50	32.1	0	0	2.63

[a] Polymerization under the condition of NCA (1.91 mmol):amine = 191:1 (molar ratio) in 10 ml of dioxane at 30°. [b] In CCl_2HCOOH at 25°.

The conversion *vs.* time plot in the polymerization of DL-Ala-NCA initiated by *dl*-Ni catalyst at 25° is shown in Figure 3, for the case of the very high catalyst concentration: molar ratio of NCA:Ni = 2 or 8 and Ni:n-Bu$_3$P = 1:2. The conversion of the NCA is represented by two straight lines intersecting at about 40 min for NCA:Ni = 2, and at about 50 min for NCA:Ni = 8. In both cases, amount of the NCA consumed at the intersecting point is equimolar to the Ni salt. Thus, the fast reaction may be attributed to the initiation reaction for which either the ring opening or the decarboxylation of the NCA is considered to be present, and the slow reaction to the polymerization.

The rate of conversion of L-Ala-NCA with *dl*-Ni catalyst was measured under a condition identical with that of DL-Ala-NCA (NCA:Ni = 8 molar ratio). Similar results were obtained, except for the time required for reaching an intersecting point being slightly longer than that for DL-Ala-NCA. This difference can be interpreted by assuming that either *d* or *l* species in the *dl*-Ni catalyst is more reactive toward D-NCA than toward L-NCA.

These experimental results on NCA show the *dl*-Ni catalyst as being different in its behavior from amine catalyst and the former as originating from the configurational factor attached to Ni atom and/or from the polymerization mechanism.

II. DL-Copolymerization of L- and DL-BG-NCA with *dl*-Ni Catalyst. The unique property of the Ni catalyst was substantiated also independently by main-chain conformation.

A. Specific Residue Rotation of the DL Copolymer. To know the stereoselecting capacity of the *dl*-Ni catalyst, L-

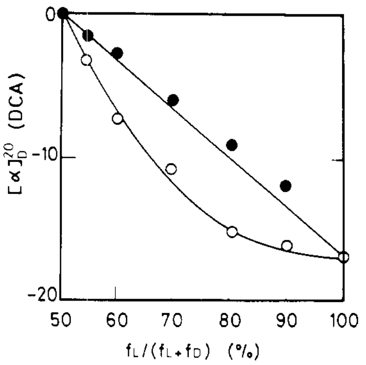

Figure 4. Relation between specific residue rotation of polymer and $f_L/(f_L + f_D)$. Circles are observed values (c = 3 g of polymer/100 ml of CCl_2HCOOH) for polymers prepared by amine catalyst (●) and those by nickel catalyst (○). Solid lines are calculated ones: A with eq 8 and B with eq 9.

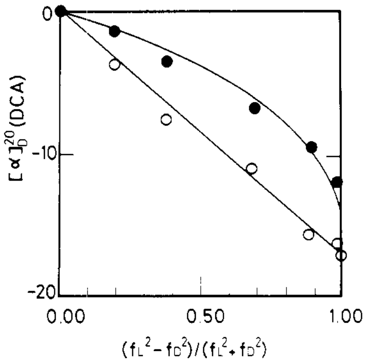

Figure 5. Relation between specific residue rotation of polymer and $(f_L^2 - f_D^2)/(f_L^2 + f_D^2)$. Circles are observed values (c = 3 g of polymer/100 ml of CCl_2HCOOH) for polymers prepared by amine catalyst (●) and those by nickel catalyst (○).

and DL-BG-NCA were copolymerized in various molar ratios using the *dl*-Ni catalyst or benzylamine.[17] The polymerization results are summerized in Tables I and II.

Specific residue rotation of P-L-BG measured in dichloroacetic acid solution can be regarded as a measure of the relative content of L- and D-monomer residue in the polymer sample, because in this coil solvent the residue rotation is reasonably assumed to be independent of absolute configuration of both its adjacent residues owing to the high molecular weight polymer formed. The specific residue rotation is plotted as a function of the monomer feed composition $f_L/(f_L + f_D)$, in which f_L and f_D denote the mole fractions of L and D monomers used for the copolymerization experiment. The plot is linear for the polymer obtained with the amine catalyst, while not linear for that with the *dl*-Ni catalyst (Figure 4).

The DL copolymerization can be regarded as a special case of the usual copolymerization reaction of two different monomers. An usual polymer composition equation[18,19] therefore can be applied to the present cases in the form of

$$-d[L]/-d[D] = ([L]/[D])(r_1[L] + [D])/([L] + r_2[D]) \quad (6)$$

where $r_1 = k_{LL}/k_{LD}$ and $r_2 = k_{DD}/k_{DL}$. In the region where the copolymer yield is low, the ratio F_L/F_D of the mole fractions of the L- and D-monomeric units in the polymer is nearly equal to $-d[L]/-d[D]$, and the initial mole fractions of the L and D monomers (f_L and f_D) are nearly equal to [L] and [D]. Equation 6 is hence represented by

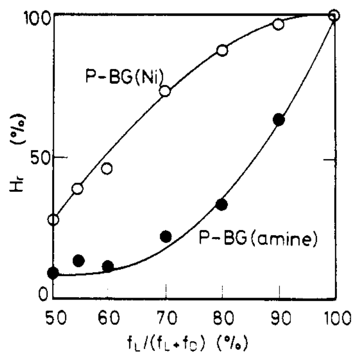

Figure 6. Relation between the content of regular helix H_r and $f_L/(f_L + f_D)$.

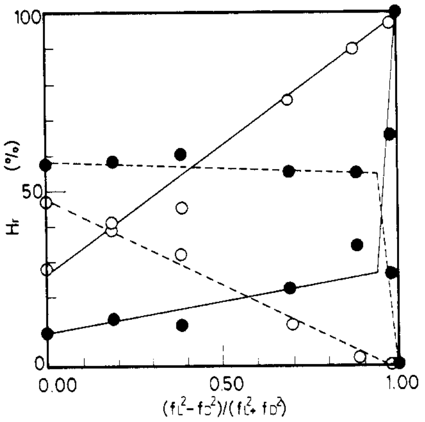

Figure 7. Plot of the content of regular helix H_r and perturbed helix H_p as functions of $(f_L^2 - f_D^2)/(f_L^2 + f_D^2)$, for polymers prepared by amine catalyst (●) and those by nickel catalyst (○). The broken line and the solid line represent H_p and H_r, respectively.

$$F_L/F_D = (f_L/f_D)(r_1 f_L + f_D)/(f_L + r_2 f_D) \quad (7)$$

Two extreme cases can be considered for the copolymerization. First, assuming $k_{LL} = k_{DD} = k_{DL} = k_{LD}$, *i.e.*, random copolymerization, eq 7 becomes $r_1 = r_2 = 1$ and $F_L/F_D = f_L/f_D$. In this case, the specific rotation measured in dichloroacetic acid solution should be expressed by

$$[\alpha]^{20}{}_D = \text{const}(F_L - F_D)/(F_L + F_D) = \text{const}(f_L - f_D)/(f_L + f_D) \quad (8)$$

The polymers obtained with amine catalyst fall on a straight line corresponding to eq 8, while those with *dl*-Ni catalyst do not (see Figure 4).

Second, assuming $k_{LL} = k_{DD} \gg k_{LD} = k_{DL}$, *i.e.*, stereoselective polymerization, eq 8 becomes $(1/r_1) = (1/r_2) \ll 1$ and $F_L/F_D = f_L^2/f_D^2$. In this case, the specific rotation measured in dichloroacetic acid solution should be expressed by

$$[\alpha]^{20}{}_D = \text{const}(F_L - F_D)/(F_L - F_D) = \text{const}(f_L^2 - f_D^2)/(f_L^2 + f_D^2) \quad (9)$$

The polymers obtained with *dl*-Ni catalyst fall on a straight line drawn by eq 9, while those with amine catalyst do not.

These experimental results shown in Figures 4 and 5 lead to the conclusion that the polymer (amine) is a random DL copolymer (or perturbed polymer) and the polymer (Ni) is a stereoblock DL copolymer (or a mixture of D

Table III
Characteristics of Polymer

	f_L[a] (%)	F_L[b] (%)	Regular Helix (%)	Perturbed Helix (%)	Random Coil (%)		f_L[a] (%)	F_L[b] (%)	Regular Helix (%)	Perturbed Helix (%)	Random Coil (%)
N-1	100	100	100	0	0	A-1	100	100	100	0	0
N-2	90	97	98	0	5	A-2	90	86	64	25	12
N-3	80	94	88	2	10	A-3	80	78	34	54	14
N-4	70	78	76	11	17	A-4	70	70	22	53	26
N-5	60	73	45	32	24	A-5	60	59	11	60	30
N-6	55	61	39	38	24	A-6	55	55	12	60	29
N-7	50	50	28	46	27	A-7	50	50	10	58	30

[a] Component of L-NCA. [b] Amount of L residues in polymer calculated from eq 9.

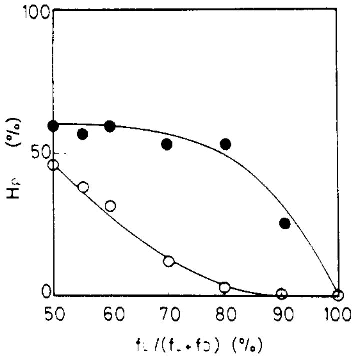

Figure 8. Perturbed helix content H_p calculated from the difference between D_{615}/D_{580} and D_{563}/D_{580}: (○) polymers prepared by nickel catalyst; (●) polymers by benzylamine catalyst.

and L homopolymers). The degree of stereoregularity of the polymer, unfortunately, cannot be derived accurately from the specific rotation measurements for two reasons. First, the observed optical rotation is so small that contribution of an experimental error is significantly large. Second, the experimental values approach eq 9 very soon (*e.g.*, $(1/r_1) = (1/r_2) = 1/4$ or so), and may be difficult to strictly distinguish from the ideal case.

B. Chain Conformation of the DL Copolymer. The possible use of main-chain conformation of polymer was examined for evaluating the degree of stereoregularity of DL copolymer quantitatively. For this purpose, ir spectroscopic intensity was applied.

Careful examination of ir absorption in the range of 1500-1600 cm^{-1} led us to the conclusion that the present DL copolymers consist of only three types of chain conformations: regular α helix, perturbed helix, and random coil.[8,20] Since the high molecular weight isotactic polymer, P-L-BG, is known to contain solely regular helix in the solid state[8] and in the helix solvent such as chloroform,[21,22] it is reasonable to assume that the degree of isotacticity (stereoregularity) of the DL copolymer parallels with the regular α-helix content.

It is known that, in the ir spectra of P-BG, the intensity of the band at 563 cm^{-1} (amide IV) parallels with the regular helix content (Hr), and that at 615 cm^{-1} (amide V) parallels with the sum of the regular helix and the perturbed helix contents $(H_r + H_p)$.[8] Following these assignments, the ir spectra of DL copolymers were analyzed. The transmittance of the polymer film prepared by casting from chloroform (helix solvent) solution is converted to the optical density, and the peaks in the region of 700-400 cm^{-1} were analyzed into two component peaks. In practice, regular helix content was determined by optical density ratio D_{563}/D_{580}, and perturbed helix content by the difference $(D_{615}/D_{580}) - (D_{563}/D_{580})$. In this case, the optical density of the band at 580 cm^{-1} was used as an internal standard, because it is assiged to the phenyl group situated in a monomeric unit. Since the present copolymer is composed of three types of chain conformations, random coil content (C_r) is easily calculated by $C_r = 1 - (H_r + H_p)$.

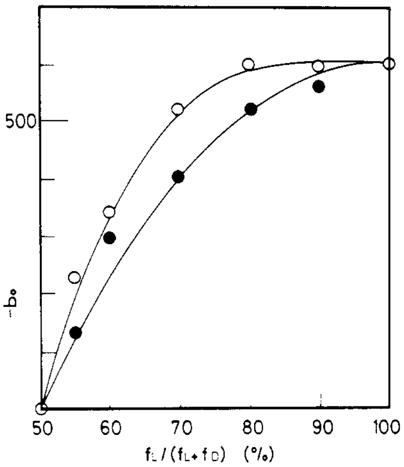

Figure 9. Plot of b_0 value of polymer as a function of $f_L/(f_L + f_D)$ for polymers prepared by amine catalyst (●) and those by nickel catalyst (○).

The regular helix content H_r was plotted against the monomer feed composition $f_L/(f_L + f_D)$ for two kinds of DL copolymers, the polymer (Ni) and the polymer (amine) (Figure 6). It can be clearly seen that the regular helix content of the former is far higher than that of the latter, in qualitative agreement with the conclusion derived from the specific rotation data mentioned above. This relationship is illustrated more clearly in the H_r *vs.* $(f_L^2 - f_D^2/Wf_L^2 + f_D^2)$ plot (Figure 7).

The perturbed helix content is plotted against the monomer feed composition (Figure 8). The perturbed helix content of the polymer (amine) is far higher than that of the polymer (Ni), just opposite the case of regular helix content. In the H_p *vs.* $(f_L^2 - f_L^2)/(f_D^2 + f_D^2)$ plot, the experimental data for the polymer (Ni) are represented by a single straight line, while those for the polymer (amine) are by two straight lines (Figure 7). It is interesting to note that, for the polymer (amine), the intersecting point of the two straight lines lies at about $f_L/(f_L + f_D) = 0.80$ for both H_r and H_p, in comparison to the identical DL-copolymerization experiments.[10]

C. Right- and Left-Handed Helix Content of the DL Copolymer. It is well known that in a helix solvent such as chloroform the difference between right- and left-handed helix contents $(H_r - H_l)$ in P-BG is represented by the b_0 value calculated by the modified Moffitt's equation (see Figure 9).[23]

The value b_0 for polymer (amine) decreases with the decrease in $f_L/(f_L + f_D)$, while that for the polymer (Ni) is almost constant in the range of 1.00-0.80 and then decreases gradually in the range of 0.80–0.50. These results agree well with the values of H_r and H_p calculated from specific rotations.

These structural analyses of DL copolymers combined with our kinetic analyses may be suggested that *dl*-Ni catalyst has a stereoselectivity for DL-NCA higher than other catalysts. This highly stereoselective capacity of *dl*-Ni catalyst suggests the asymmetric carbon atom in the acyloxy moiety of this catalyst contributes mainly to this property, because that of $Ni(OAc)_2{\cdot}4H_2O$-*n*-Bu_3P and of benzylamine is similar to each other and differs from that of nickel *dl*-2-methylbutyrate catalyst.

III. An Example of Highly Stereoregular Polymer Obtained from DL-NCA. DL-BG-NCA was polymerized in 5 wt % dioxane solution at 30° for 72 hr with the *dl*-Ni catalyst (molar ratio, NCA:Ni:P = 4:1:11.8) after aging at 30° for 25 min. The polymer obtained in 79.5% yield had a molecular weight of 5.98×10^4 and was composed of the regular and perturbed helixes in a ratio of 90:10. This value of chain conformation is independently supported quantitatively by the surface pressure *vs.* surface area relationship obtained by the monolayer methods using our samples.[24] Highly stereoregular polyalanine was also obtained from DL-Ala-NCA with the *dl*-Ni catalyst in 5 wt % anisole solution.

The stereoselective polymerization of DL-BG- and of DL-Ala-NCA with *dl*-Ni catalyst was extended to the stereoelective (or asymmetric) polymerization of DL-BG- and of DL-Ala-NCA with *d*-Ni catalyst. This extension gave optically active polymers fully supporting our evidence, and will appear in a subsequent paper.

References and Notes

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Superacids and Their Derivatives. IV.[1] Kinetic Studies on the Ring-Opening Polymerization of Tetrahydrofuran Initiated with Ethyl Trifluoromethanesulfonate by Means of ^{19}F and ^1H Nuclear Magnetic Resonance Spectroscopy. Evidence for the Oxonium–Ester Equilibrium of the Propagating Species

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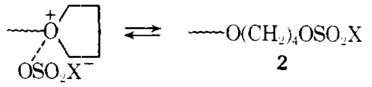
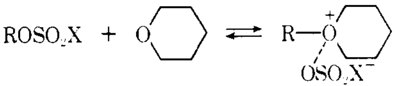
ABSTRACT: Kinetic studies on the ring-opening polymerization of tetrahydrofuran (THF) initiated with ethyl trifluoromethanesulfonate ($EtOSO_2CF_3$) were performed by means of ^{19}F and ^1H nmr spectroscopy. The equilibrium between the oxonium (**3**) and ester (**4**) species of propagation was directly observed by ^{19}F nmr spectroscopy. Solvent effect on the polymerization was examined in five solvents of CCl_4, $CHCl_3$, CH_2Cl_2, benzene, and nitrobenzene. The fraction of the oxonium ion concentration, $[O^+]$, was increased in polar solvents, and *vice versa.* Rate constants of initiation (k_i) and propagation due to **3** ($k_{p(i)}$) and apparent rate constants of propagation ($k_{p(ap)}$) were determined on the basis of the direct determination of the instantaneous concentrations of **3**, **4**, and monomer by ^{19}F and ^1H nmr spectroscopy. Rate constants of propagation due to the ester **4** ($k_{p(e)}$) were estimated to be very small compared with $k_{p(i)}$. The activation parameters of the elementary reactions were determined in CCl_4 solvent.

Very recently we have reported kinetic studies on the cationic ring-opening polymerization of tetrahydrofuran (THF) initiated by superacid esters[2] and anhydrides.[3] In these studies, the oxonium–ester equilibrium of propagating species (eq 1) has been discussed.[2]


(1)

1 (X = CF_3, F, Cl) 2

In addition, such equilibrium has already been established in the reactions of superacid esters with tetrahydropyran (eq 2).[1,4]


(2)

In the previous study by proton nmr (^1H nmr) spectroscopy,[2] however, it was very difficult to verify directly the