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MECHANISTIC FEATURES OF POLYMERIZATION OF *N*-CARBOXY-α-AMINOACID ANHYDRIDES— COMPARISON WITH THOSE OF 1,2-EPOXIDES

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Abstract—This paper reviews recent results of our studies on (1) polymerization mechanism of α-aminoacid NCA with organozinc compounds, (2) asymmetric selective polymerization of α-alanine NCA with organoaluminum initiators, (3) circular dichroism studies on the polymerizations of γ-benzyl glutamate NCA and valine NCA, (4) stereoselective and asymmetric selective polymerizations of tert-butylethylene oxide, and (5) comparison of the modes of stereoselection. This review intends to clarify the points of difference and of similarity among a variety of the stereochemical features exhibited by polymerization reactions of α-aminoacid NCA and epoxides induced by several types of initiators.

N-Carboxy-α-aminoacid anhydrides (α-aminoacid NCA) has long been known to be polymerized and form polypeptides with various types of initiator such as amine, water, alkali alcoholate, and lithium chloride. Few papers, however, had been available on the NCA-polymerization by means of organometallic initiators before our first paper[1] appeared. Mechanistic studies on the organozinc (or aluminum)-initiated NCA polymerization led us to the concept of an "activated monomer" as the operative species which was formed through metallation reaction of NCA by zinc (or aluminum) alkyl.

It was previously shown[2] that organozinc compounds exhibited an excellent stereoselective behavior as catalyst in the polymerization of 1-substituted-1,2-epoxide such as propylene oxide. The mechanism of the stereoselection was interpreted in terms of the enantiomorphic catalyst sites model.[2] One of the common stereochemical features of α-aminoacid NCA and propylene oxide is that these two monomers possess an asymmetric carbon atom for each molecule. The stereochemistry of the organometal-initiated NCA polymerization was studied in comparison with that of the 1,2-epoxide.

Alkali alkoxide (or hydroxide), contrary to the organozinc (or aluminum) catalyst, was proven previously to be a non-stereoselective catalyst for propylene oxide polymerization. In the polymerization of some α-aminoacid NCA, however, alkali alkoxide or amine could become an initiator of polymerization in which α-helical structure of the growing chain makes an essential contribution to the stereoselection of incoming monomers. With the aid of circular dichroism measurements of the polymerization system, it was shown directly that the stereoselection of the monomer antipodes was closely related with the chiral structure of α-helices of the growing polypeptide chains. Another example of the stereoselection caused by a chiral growing chain was found, for the first time, in the polymerization of tert-butylethylene oxide using potassium tert-butoxide as initiator. Bulkiness of tert-butyl group of the epoxide seemed responsible for its unique behavior in the stereoselective polymerization.

This paper reviews recent results of our studies on (1) polymerization mechanism of α-aminoacid NCA with organozinc compounds, (2) asymmetric selective polymerization of α-alanine NCA with organoaluminum initiators, (3) circular dichroism studies on the polymerizations of γ-benzyl glutamate NCA and valine NCA, (4) stereoselective and asymmetric selective polymerizations of tert-butylethylene oxide, and (5) comparison of the modes of stereoselection.

The author intends by this review to clarify the points of difference and of similarity among a variety of the stereochemical features exhibited by polymerization reactions of α-aminoacid NCA and epoxides induced by several types of initiator.

1. *Polymerization mechanism of α-aminoacid NCA with organozinc compounds*

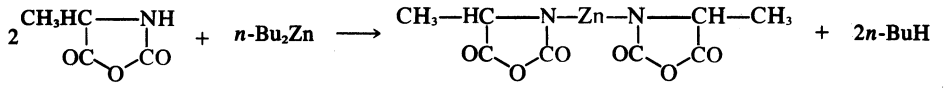
α-Alanine NCA can be polymerized with various organometallic initiators including those of lithium, magnesium, aluminum, zinc and cadmium. The first step of the dibutylzinc-initiated polymerization of alanine NCA was concluded to be a proton abstraction reaction to form a metallated alanine NCA.[3]

This conclusion was based on the following results: Infrared spectrum of the equimolar mixture of di-*n*-butylzinc and DL-alanine NCA showed the complete disappearance of absorption bands of ν_{NH} (3240 cm^{-1}) and ν_{CO} (1840 cm^{-1} and 1780 cm^{-1}), which were assignable to the free DL-alanine NCA. The occurrence of the proton abstraction reaction was also confirmed by "drying up" treatment, in which volatile materials were removed from the reaction mixture under reduced pressure at room temperature. After a suitable amount of solvent was added to the residue, the mixture was acidified by addition of excess acetic acid to release *n*-butane from unchanged *n*-Bu–Zn bonds.

When di-*n*-butylzinc was mixed with excess of NCA, *n*-butane was recovered quantitatively without the drying up procedure, which indicated that carbonyl addition reactions of di-*n*-butylzinc to DL-alanine NCA did not take place. No *n*-butane was recovered, however, from the reaction mixture after the drying up treatment which meant the complete consumption of the two *n*-butyl groups of di-*n*-butylzinc by the proton abstraction reaction.

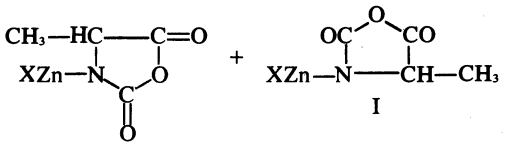
From these results, the first step of the reaction of di-*n*-butylzinc with excess of DL-alanine NCA can be concluded as shown at the top of the next page.

To study the reactivity of the metallated NCA, I, in the propagation stage, sarcosine NCA was used as a reference monomer. A ternary system consisting of DL-alanine NCA, sarcosine NCA and I was easily obtainable by adding *n*-Bu_2Zn to an equimolar mixture of DL-alanine NCA and sarcosine NCA in 3–10 mol ratio. Infrared studies on the



I

ternary system showed that the intensity of a band (920 cm^{-1}) assignable to DL-alanine NCA decreased with time in contrast with the unchanged intensity of bands (980 cm^{-1} and 900 cm^{-1}) assignable to sarcosine NCA. The result suggested that I was not able to undergo an addition reaction onto the carbonyl group of sarcosine NCA. Since the reactivity of carbonyl group of free DL-alanine NCA is not considered much different from that of sarcosine NCA, it was postulated that the operative species in the propagation stage should be the metallated NCA, I:



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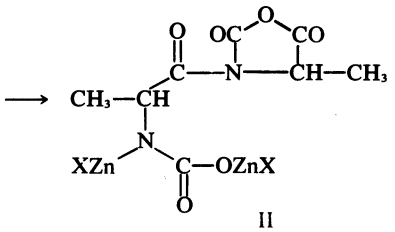
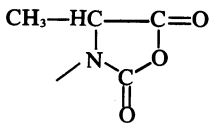
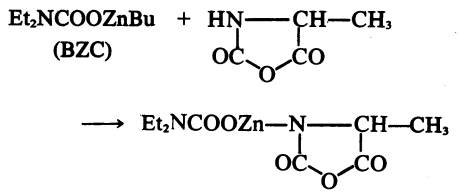


II

where X is



A model compound, III, for the propagating species II could be formed by a reaction between *n*-butylzinc *N,N*-diethylcarbamide (BZC) and DL-alanine NCA:

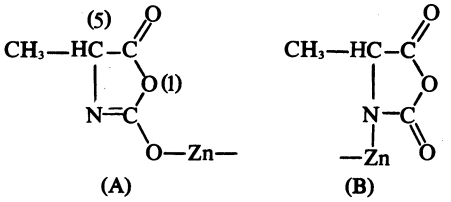


III

The validity of this reaction was confirmed by the analysis of *n*-butylzinc bond by acetyl chloride. The acyl chloride was added to an equimolar mixture of BZC and DL-alanine NCA. *n*-Butane obtained from the reaction mixture without the acidification was almost quantitative, which indicated that *n*-butyl group of BZC underwent proton abstraction reaction with DL-alanine NCA, but not carbonyl addition reaction.

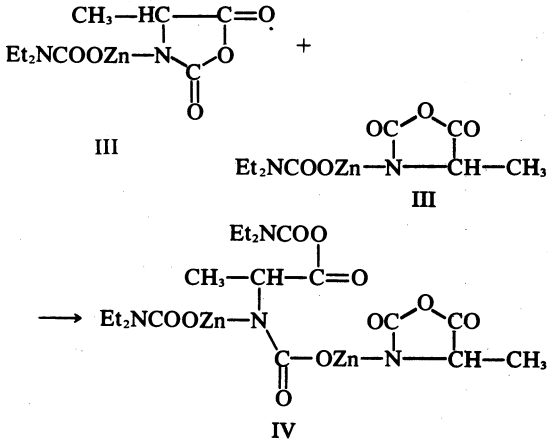
To trace the fate of the model compound, III, for the propagating species of the NCA polymerization, i.r. spectra of an equimolar reaction mixture between BZC and DL-alanine NCA were studied. The results showed that the absorption bands of ν_{CO} and ν_{NH} of the NCA disappeared rapidly and some new bands appeared between 1900 cm^{-1} and 1500 cm^{-1}, and changed their intensity remarkably with time. These absorption bands were (a) 1840 cm^{-1}, (b) 1825 cm^{-1}, (c) 1760 cm^{-1}, (d) 1680 cm^{-1}, (e) 1610 cm^{-1}, and (f) 1560 cm^{-1}. On mixing BZC with DL-alanine NCA bands (b) and (d) appeared and at the same time ν_{CO} bands of free DL-alanine NCA disappeared. New bands (a), (c), (e) and (f) appeared later and their absorbance increased at the expense of bands (b) and (d). After about 10 hr, absorptions (a) and (c) began to decrease with appearance of ν_{CO} absorption band of carbon dioxide at 2380 cm^{-1}, and faded away after several days.

Bands (b) and (d) were concluded to be assigned to ν_{CO} of the metallated NCA. When compared with ν_{CO} of free α-aminoacid NCA, bands (b) and (d) shifted to lower wave number, a fact which suggested the structure of the metallated NCA to be (A) rather than (B).



(A) (B)

The carbonyl-carbon at 5-position of the metallated NCA was considered to be activated enough to accept a nucleophilic attack.



III

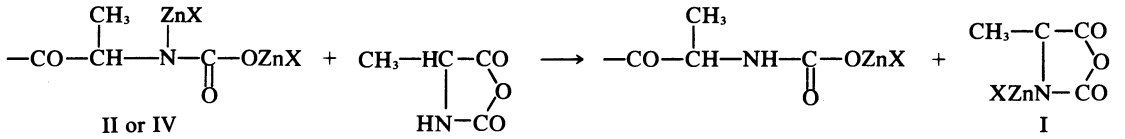
IV

Bands (a) and (c) are evidently due to ν_{CO} of the mixed anhydride bond as shown in IV, which changes to amide group eliminating carbon dioxide. Bands (e) and (f) are presumably considered to be ascribed to the newly formed amide group.

In the reaction system of the NCA polymerization, the metallated monomer molecules are generated by the reaction with II or IV.

The acidity of -NH-COOZnX group in II or IV is expected to be lower than that of NH in the NCA owing to the electropositive nature of Zn atom in the carbamate group.

The newly generated metallated NCA will be ready to accept the attack of the zinc carbamate locating at the growing chain end. It is clear from the above discussion



II or IV

I

that the metallated NCA is the operative species in the propagation reaction. In this sense, the metallated NCA can be regarded as an "activated monomer".

The concept of an "activated monomer" was advanced[4-6] previously for the elucidation of mechanism of NCA polymerization initiated by strong bases, in which "activated NCA" was assumed to undergo the addition reaction onto the carbonyl group of free NCA molecules. Harwood and Seeney,[7] however, have recently presented results that led us to believe that both weak and strong base initiated NCA polymerization proceed with carbamate ions as propagating species.

Although further experimental results are required to decide which mechanism is valid for the strong base initiated NCA polymerization, it is important to point out that the both theories assume participation of free NCA monomers in the propagation stage. It was reported[8] that sarcosine NCA could be copolymerized with DL-alanine NCA with tertiary amines or alkali metal alkoxides. Copolymerization between DL-alanine NCA and sarcosine NCA was not possible with dialkylzinc as initiator, only polyalanine being formed with unchanged sarcosine NCA remaining in the reaction system.

2. *Asymmetric selective polymerization of α-alanine NCA with organoaluminum initiators*[9]

1,2-Epoxides such as ethylene oxide or propylene oxide are not polymerized with dialkylzinc alone as initiator. The active initiating species[2] in the Et_2Zn–MeOH catalyst was shown to be $Zn(OMe)_2$. The mechanism of stereoselective polymerization of DL-propylene oxide induced by $Zn(OMe)_2$ was elucidated[2] previously in terms of the enantiomorphic catalyst sites model in which the stereocontrol of polymerizing monomer molecules is effected by the chiral nature of catalyst sites, but not by that of the growing chain ends. This conclusion was based on various experimental evidences. Especially, characteristics of copolymerization between D- and L-monomers afforded useful information on the stereocontrol mechanisms. In accordance with the enantiomorphic catalyst sites model, D- and L-propylene oxide monomers were copolymerized in exactly the same D/L ratio as in the starting monomer mixtures.

It was noticed previously[1] the formation of a water-insoluble polymer when aluminum alkyl was used as initiator in the polymerization of DL-alanine NCA. The water-insoluble polyalanine was found to possess some stereoregular structure. In order to elucidate the mechanism of the stereoselective polymerization of DL-alanine NCA, D- and L-copolymerization was studied using triethylaluminum and diisobutylaluminum diethylamide as initiator.

In the copolymerization of D- and L-alanine NCA with an excess of L-antipode by triethylaluminum, a polyalanine containing an equal amount of L- and D-residues was obtained in the early stage of the polymerization, though no racemization took place throughout the polymerization process. After this early stage, the L-content in the non-reacting NCA continued to decrease with the progress of the copolymerization reaction, and in the final stage it attained lower values than the L-unit content of the polymer phase of that stage (Fig. 1).

By analysis of the data presented in Fig. 1, it was concluded that the stereocontrol in the asymmetric selective polymerization is effectuated by the chiral nature of the growing chain ends. The monomer reactivity ratio, k_{LL}/k_{LD} (or k_{DD}/k_{DL}), obtained from the data was 2.1 ± 0.3.

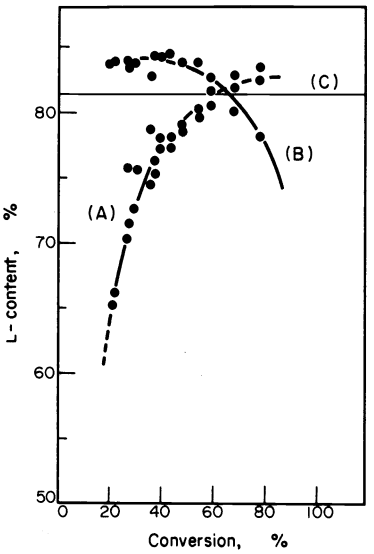
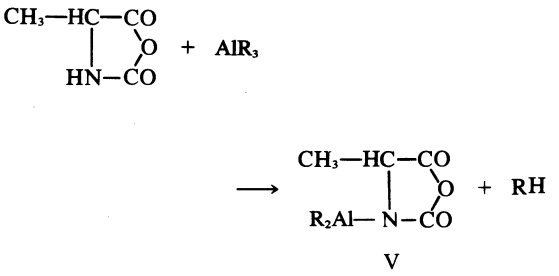


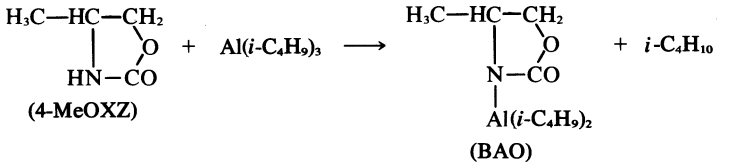
Fig. 1. Correlation between L-unit content of polymer and unreacted *N*-carboxy-α-amino acid anhydride (NCA) for conversion of alanine-NCA polymerization with $AlEt_3$. (A): Poly-alanine; (B): Unreacted NCA; (C): L-content of starting NCA (81.4%), solvent: THF, NCA concentration: 0.24 g · ml^{-1}, NCA/$AlEt_3$: 40, reaction temp.: 30°C.

It was confirmed by the NMR study on the polymerization system that in the early stage of the polymerization, only one isobutyl group was consumed by a proton abstraction reaction:

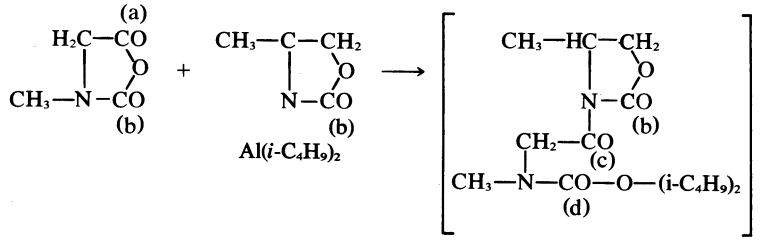


V

To elucidate the stereochemistry of the NCA polymerization initiated with trialkylaluminum, a model compound, diisobutylaluminum 4-methyloxazolidonate (BAO), was prepared:[10]



BAO reacted smoothly with sarcosine NCA in dioxane at 30°C. Changes with time in the i.r. spectra of the equimolar reaction mixture of BAO and sarcosine NCA could be interpreted in terms of the following scheme:



(sarcosine NCA)
(a) 1860 cm^{-1}
(b) 1785 cm^{-1}

(BAO)
(b) 1665 cm^{-1}

(VI)
(b) 1785 cm^{-1}
(c) 1715 cm^{-1}
(d) 1550 cm^{-1}

It was to be noted that (VI) had no longer any reactivities toward sarcosine NCA in spite of its excellent ability to initiate the polymerization of alanine NCA. Diisobutylaluminum *N,N*-diethylcarbamate behaved similarly to (VI) toward salcosine NCA and alanine NCA.

These facts show that the aluminum carbamate is lacking the ability of direct addition to the carbonyl group of free NCA, and the proton abstraction reaction from NH group of an NCA by the carbamate group is a prerequisite step for the polymerization reaction of the NCA in a similar way to the reactions with organozinc initiators.

Since the stereochemical control of the polymerization should be determined by the stereospecificity involved in the reaction of the metallated NCA, the stereochemical behaviors of BAO were examined as a model compound of the metallated NCA.

The degree of association of L- and DL-BAO was determined by cryoscopic method in the presence of 4-methyl-oxazolidone-2(4-MeOXZ). Results obtained indicated that BAO species were present as dimeric forms and that there were some complexation of BAO dimer with 4-MeOXZ. I.R. NMR and ORD studies on dioxane solutions of L- and DL-BAO also supported the existence of their associated forms.

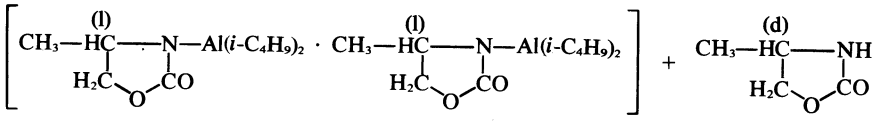
There should be considered for BAO two types of diastereoisomeric dimer, active-dimer and *meso*-dimer. To determine the relative stability of the two types of dimer, exchange reactions of 4-MeOXZ residue were examined between BAO and free 4-MeOXZ.

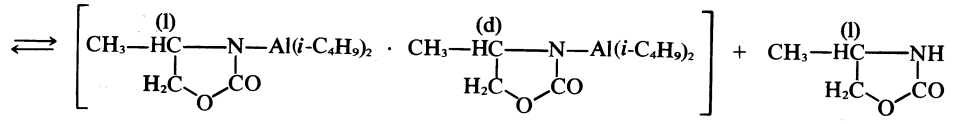
The optical rotation of the recovered 4-MeOXZ from BAO was found to be always smaller and that of free 4-MeOXZ was always larger than the overall optical rotation. It was concluded therefore that, in the dimeric forms of BAO, the structure having alternative chirality in 4MeOXZ residue (*meso*-dimer) was more stable than that having the same chirality (active-dimer).

On the basis of the experimental results on the model compound, BAO, the mechanism of the stereocontrol in the early stage of the alanine NCA polymerization was considered as follows.

Since the contribution of growing polymer chain to the stereoselective reaction should be practically negligible in the early stage of polymerization, the metallated NCA should play the major role in the stereoselective reaction. The metallated NCA was presumably associated with each other to form dimeric structure in the presence of free NCA, similarly to the association behavior of BAO. In the dimeric structures of the metallated NCA, the preference of *meso*-dimer to active-dimer was again considered. The produced polymer in the early stage of the polymerization through the metallated NCA dimer (predominantly *meso*-form) should consist of almost equal amount of L- and D-residues, independently of the optical purity of coexisting NCA monomer.

When a growing polymer chain propagates to some extent, the polymer chain interacts with the metallated NCA. The steric control is considered to take place by steric cooperations between the ultimate unit and the incoming NCA through the coordination of aluminum





atom, in consistence with the growing chain end control mechanism.

3. *Circular dichroism studies on the polymerizations of γ-benzyl glutamate NCA and valine NCA*

We examined previously the D- and L-copolymerization of alanine NCA[11] and that of γ-benzyl glutamate NCA.[12] The observed stereoselection was discussed in terms of the α-helix formation during the polymerization. In order to obtain direct information about the secondary structure of the polymer molecules being formed in the reaction system, the behavior of the secondary structure of growing polymer chains was examined by means of circular dichroism (CD) of the reaction solution.[13] The strength of the CD peak at 222 nm was taken as a measure for the helical structure, more strictly the difference of the content of the right-handed and the left-handed α-helices. In the CD measurement, it was essential to examine a possible contribution of the β-structure to the CD band, because the latter structure exhibited a large CD peak in the vicinity of 222 nm (at 218 nm). A check of the β-structure was made by means of i.r. spectroscopy.

The D- and L-copolymerizations of γ-benzyl glutamate NCA were carried out in 1,2-dichloroethane at 30°C with *n*-$BuNH_2$ or CH_3ONa as initiator. In the reaction solution (0.1 mol/l) the β-structure peak was clearly observed in the early stages by i.r. spectroscopy at 1630 cm^{-1}. At 25–30% conversion the peak was observed as only a shoulder, which suggested that the β-structure was virtually absent during the middle and later stages of the polymerization.

To esimate the molar ellipticity at 222 nm, $[\theta]_{222}$, per amino acid residue introduced into polymer chains, observed values of the ellipticity were divided by the conversion at each stage of the polymerization. Figure 2 shows the correlation between $[\theta]_{222}$ per amino acid residue and conversion in the polymerization system initiated by *n*-butylamine. In the 100%-L-monomer system the molar ellipticity per amino acid residue in polymer molecules (α-helix) is constant throughout the polymerization process examined.

On the other hand, in the 65%-L-monomer system the molar ellipticity increases gradually with conversion. The results indicate that the amino acid units introduced into polymer chains make a rather low contribution to the α-helical structure in the early stage of the polymerization, while they make a gradually increasing contribution to the α-helical structure in later stages. This result is consistent with our previous data[11,12] by the ORD spectroscopy.

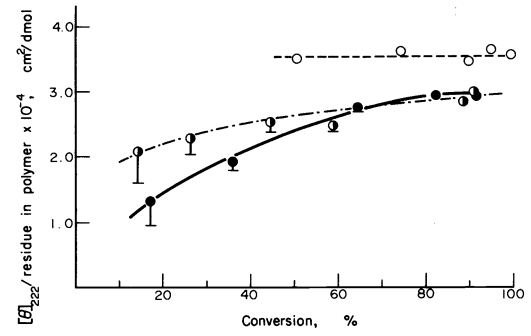


Fig. 2. The conversion vs the molar ellipticity per amino acid residue in polymer molecules. *n*-Butylamine system. (--○--) L 100%, $[A]_0/[I]_0 = 40$; value corrected for NCA. (—●—) L 65%, $[A]_0/[I]_0 = 40$. (—·♀—·) L 65%, $[A]_0/[I]_0 = 80$. Each plot represents the observed value (●, ◑) and the corrected value for maximum possible contribution of NCA (−).

In the polymerization of NCA initiated by sodium methoxide, the average degree of polymerization remains constant throughout every stage of the polymerization process. In addition, the rate of polymerization is much higher than in the polymerization initiated by *n*-butylamine.

Figure 3 shows the correlation between the molar ellipticity per amino acid residue in the polymer at 222 nm and the conversion of polymerization initiated by sodium methoxide.

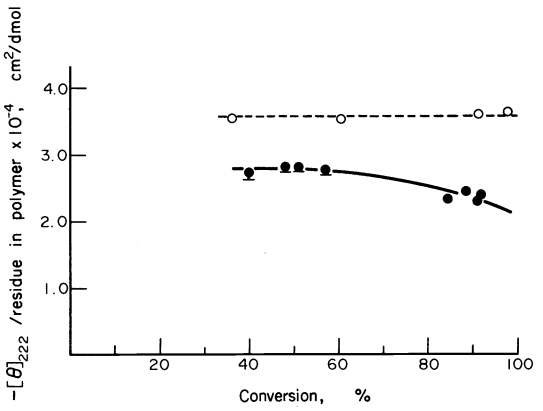


Fig. 3. The conversion vs the molar ellipticity per amino acid residue in polymer molecules. Sodium methoxide system. (--○--) L 100%, $[A]_0/[I]_0 = 40$; value corrected for NCA. (—●—) L 65%, $[A]_0/[I]_0 = 40$. Each plot represents the observed value (●) and the corrected value for maximum possible contribution of NCA (−).

Figure 3 indicates that in the 100%-L-monomer system, once the α-helical structure is formed, successive monomer units introduced into a polymer chain make a constant high contribution to the α-helical structure. In the 65% L-monomer system, on the other hand, the molar ellipticity per amino acid residue in polymer molecules is very high in the early stage of polymerization, but tends to decrease in later stages. This fact means that the growth in the left handed α-helical structure can no longer be negligible in the later stages, because the reaction system becomes relatively rich in D-antipodes owing to the preferential consumption of L-antipodes by right handed α-helical polymers in the earlier stages.

It was concluded from these results that the stereoselectivity of the growing chain ends is different from each other in response to the nature of initiator used for the polymerization.

To examine, from another viewpoint, the role of helical structure in the stereocontrol in NCA polymerization, a series of D and L copolymerizations were carried out with valine NCA,[14] the growing polymer chains of which were considered to take β-like conformation. The copolymerizations were initiated by *n*-butylamine, and 1,2-dichloroethane (DCE)or *N,N*-dimethylformamide (DMF) was used as solvent for the polymerization.

The polymerizations proceeded in heterogeneous systems owing to the insolubility of the polymer formed. The polymerization stopped at about 60% conversion in DMF, while it proceeded to 100% in DCE, where the polymers formed were apparently swelled.

In the reaction systems of 75% L in feed monomer in DMF and of 80% L in DCE, the values of the specific rotation, $[\alpha]_{589}$, did scarcely vary at any conversion as shown in Fig. 4.

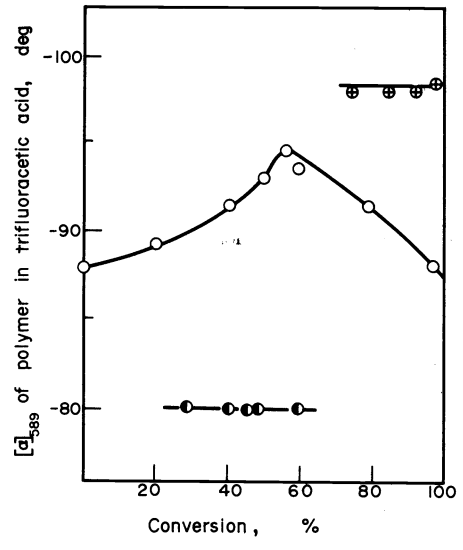


Fig. 4. $[\alpha]_{589}$ of polypeptides in trifluoroacetic acid (TFA) vs conversion of polymerization of (⊕) valine NCA in DCE (L 80% in feed monomer); (◐) valine NCA in DMF (L 75% in feed monomer); (○) alanine NCA in THF (L 77.3% in feed monomer).

The specific rotation, $[\alpha]_{589}$, in trifluoroacetic acid of the polymer formed was plotted against the L-content of feed monomer (Fig. 5). The plot formed a straight line irrespective of the conversion. The results are expressed by eqn (1):

$$\frac{d[D]}{d[L]} = \frac{[D]}{[L]}. \qquad (1)$$

The relation of eqn (1) can be explained in terms of a non-selective incorporation of D- and L- antipodes into growing polymer chains.

The non-stereoselective features of the polymerization of valine NCA was ascribed to the lack of helical structure of the growing peptide chains.

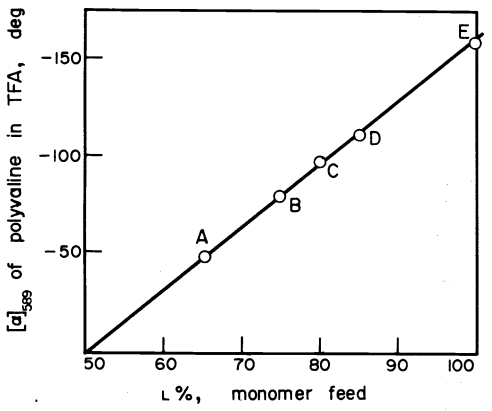


Fig. 5. $[\alpha]_{589}$ of poly-valine in TFA vs L-content of feed monomer (A) L65% (in DMF; conversion 48%); (B) L75% (in DMF; conversion 29 ~ 60%); (C) L80% (in DCE; conversion 76 ~ 100%); (D) L85% (in DMF; conversion 52%) and (E) L100% (in DCE; conversion 100%).

In harmony with this, infrared studies suggested that the stability of the main chain conformation, antiparallel β-structure, of poly-L-valine did not vary seriously with the introduction of D-antipodes.

The alternative explanation of eqn (1), however, may be possible by the concept of the enantiomorphic catalyst sites model, if the chain growth is assumed to take place at d- and l-catalyst sites which are present in an equal number (cf. Section 5).

In the polymerization of α-aminoacid NCA initiated by primary amine, the initiation reaction is much faster than the propagation reaction. The growing species formed are known to possess the same D/L ratio as the feed monomer. Therefore, the formation of an enantiomorphic catalyst sites is considered most improbable for the polymerization system of valine NCA initiated by *n*-butylamine.

4. *Stereoselective and asymmetric selective polymerization of tert-butylethylene oxide*

It was previously reported that no stereoselection took place in the copolymerization of D- and L-propylene oxide when KOH or KOR was used as initiator. Price[15–17] polymerized (RS)-*t*-butylethylene oxide with *t*-BuOK as initiator. He showed that the poly(*t*-BuEO) formed possesses *isosyn* enchainments such as -RRSSRRSS- Price proposed a growing chain control mechanism in which the bulky *t*-butyl substituents were assumed to restrict the relative modes of orientation of an incoming monomer against the chiral chelate ring composed of two units of the growing chain end.

To elucidate the reaction mechanism of the *t*-BuEO polymerization, R- and S- copolymerizations were carried out in bulk at 60°C with *t*-BuOK as initiator.[18] Two significant features of results were obtained in the bulk copolymerization. As shown in Fig. 6, the plots of the molecular, weight of the polymer obtained vs the conversion gave a straight line, indicating that the copolymerization proceeded according to the "living" mechanism with 100% initiator efficiency.

Figure 7 shows that the optical rotation of the unreacted monomer in the reaction mixture decreased rapidly as the polymerization proceeded. No racemization of the

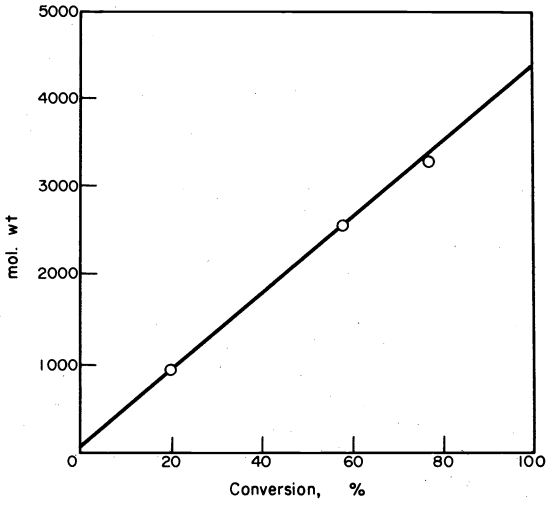


Fig. 6. Molecular weight of the polymer obtained at various conversions in the tert-BuOK-initiated bulk copolymerization of (R)- and (S)-tert-BuEOs at 60°C: mole ratio of tert-BuOK to monomer 0.019.

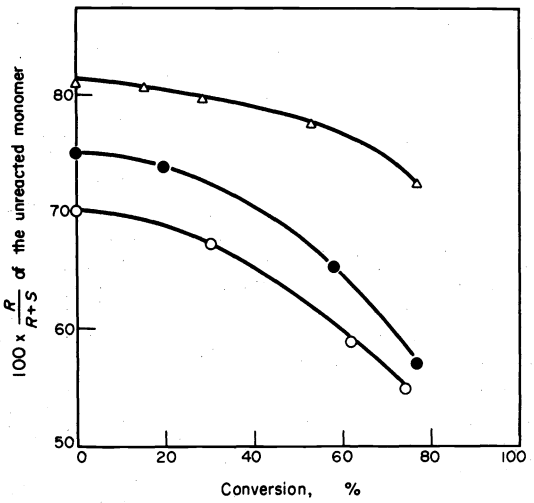


Fig. 7. The amounts of (R)-antipode, 100(R)/[(R) + (S)], in the unreacted monomer recovered from the reaction system of tert-BuOK-initiated bulk copolymerization of (R)- and (S)-tert-BuEOs at 60°C; mole ratio of tert-BuOK to monomer 0.015 (○, △) and 0.019 (●).

of the unreacted monomer can be expected as the polymerization proceeds. Our results Fig. 7 do not meet this expectation, indicating that the *isosyn* mechanism does not operate when either of the antipodes is in excess in the polymerization system.

Thus, a reasonable interpretation of the results in Fig. 7 is a growing chain control mechanism: when (R)-monomers are in excess in the polymerization system, a growing chain end moiety consisting of a predominant amount of (R)-monomer residue is likely to take a kind of chiral structure and incorporates a (R)-monomer preferentially.

According to our conformational analysis of poly[(*R*)-tert-BuEO] in solution, more than 75% of the polymer segments take a helical structure locally and statistically due to the steric hindrance of the bulky tert-butyl side groups, in harmony with the (9/4) helical structure reported for the crystalline state.[19] In the light of these results on the conformation of poly(tert-BuEO) molecules the helical structure of the growing chain end moiety should play an important role in the chiral structure responsible for the stereoselection in the propagation process.

Our observation of asymmetric selection due to the chiral structure of the growing chain end moiety may be

Table 1. Comparison of the modes of stereoselection

Monomer	Initiator: Alkali metal alkoxide or amine	Initiator: Organoaluminum or organozinc compounds
N-Carboxy-α-amino acid anhydride	● Stereoselection by growing chain (α-helix control): e.g. α-alanine-NCA, γ-benzyl glutamate-NCA ● Non-stereoselection e.g. valine-NCA, β-benzyl aspartate-NCA	● Stereoselection by growing chain end: e.g. α-alanine NCA
	● Stereoselection by growing chain: e.g. *t*-butylethylene oxide ● Non-stereoselection: e.g. propylene oxide	● Stereoselection by enantiomorphic catalyst sites: e.g. propylene oxide, butene oxide, *t*-butylethylene oxide

monomer takes place during the polymerization because the unreacted monomer, recovered from the reaction system of *t*-BuOK-initiated homopolymerization of (R)-*t*-BuEO at about 77% conversion, showed the same specific rotation as that of the starting (R)-monomer.

In addition, the polymer isolated from the (R)- and (S)-copolymerization system showed an optical activity corresponding to the amounts of the monomer antipodes incorporated into the polymer. Therefore, the decrease in the specific rotation of the recovered monomer should be ascribed to the asymmetric-selective polymerization. Obviously, the enantiomorphic catalyst site control mechanism for stereoselective polymerization does not hold for the present copolymerization, since the recovered monomer showed a different specific rotation from that of the starting monomer.

If the *isosyn* regulation on the K^+ counter ion is strong enough even in polymerizations such as shown in Fig. 7, i.e. when the amounts of the starting (R)- and (S)-monomers are unequal, an increase in the optical rotation

the first example of a base-catalyzed polymerization of a 1,2-epoxide, the stereochemical feature of which is closely similar to that of the NCA polymerization.

5. *Comparison of the modes of stereoselection*

In the foregoing sections, features of stereoselection in the polymerizations of α-aminoacid NCA and 1,2-epoxide were discussed with the emphasis of chemical behaviors of the monomers which were varied in response to the nature of initiators used for the polymerizations.

Main features of the stereoselection are summarized in Table 1.

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