Alternating Copolymerization of 2-Oxazoline with β-Propiolactone

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ABSTRACT: This study confirms the 1:1 alternating copolymerization of 2-oxazoline (OXZ) with β-propiolactone (BPL), which proceeds without any added initiator. The structure of the 1:1 alternating copolymer is $\left(CH_2CH_2N(HC{=}O)CH_2CH_2CO_2 \right)_p$, which was established by ir and nmr spectra as well as the structure of the alkaline hydrolysis product. Also, the values of the apparent monomer reactivity ratio support the 1:1 alternating copolymerization. A new concept of alternating copolymerization is proposed, in which the betaine from OXZ and BPL adds to the end of the so-called a macrozwitterion of the propagating species.

The subject of this study is the 1:1 alternating copolymerization of 2-oxazoline (OXZ) with β-propiolactone (BPL). It is well known that 2-alkyl- and 2-aryloxazolines are polymerized by cationic initiator to produce poly(*N*-acylethylenimine).[1,2] Copolymerization between two homologues of 2-substituted-2-oxazolines has also been reported by Seeliger.[2a] There has been no report, however, on the ring-opening copolymerization of 2-oxazolines with other kinds of monomer. Recently we succeeded in polymerizing pure unsubstituted 2-oxazoline (OXZ)[3] and showed that the ring-opening reactivity of OXZ was higher than the reactivities of 2-substituted homologs.[4] In the present study it was found that the copolymerization of OXZ with BPL proceed without any added initiator to produce the 1:1 alternating copolymer. A mechanistic scheme is presented for the 1:1 alternating copolymerization, in which the betaine from OXZ and BPL is the key intermediate.

Experimental Section

Reagents. OXZ was prepared and purified as described previously.[3] 2-Methyl-2-oxazoline (MeOXZ) and 2-phenyl-2-oxazoline (PhOXZ) were prepared by the isomerization of *N*-acetyl- and *N*-benzoylethylenimines, respectively.[4] Commercial reagent grade BPL was dried over calcium hydride and distilled under reduced nitrogen pressure. *N*-Methyl-2-methyl-2-oxazolinium iodide was prepared as previously reported.[4] Pyridine–BPL betaine was synthesized by Gresham's method.[5] All solvents were purified by the usual methods and dried with Molecular Sieve 4A under nitrogen.

Polymerization Procedure. When solvent, OXZ, and BPL were admixed in a tube under nitrogen at a polymerization temperature, *e.g.*, 40°, the copolymerization commenced. The reaction mixture was kept at a constant temperature with magnetic stirring. After that, the reaction mixture was poured into ether to precipitate the polymeric product, which was then isolated by centrifugation and dried *in vacuo*.

Hydrolysis of Copolymer. To 0.05–0.06 g of copolymer was added 0.5 ml of a 10% solution of NaOH in D_2O. The hydrolysis mixture was kept at 98° for 3 hr. The reaction product was directly subjected to nmr measurement. The authentic compound *N*-(β-hydroxyethyl)-β-alanine for the alkaline hydrolysis product was prepared by the equimolar reaction of monoethanolamine and BPL as reported, mp 141–143° (lit.[5] 145–147°). *Anal.* Calcd for $C_5H_{11}NO_3$: C, 45.10; H, 8.33; N, 10.52. Found: C, 45.18; H, 8.31; N, 10.43.

Nmr Spectra. Nmr spectra were taken on Varian T-60 and HA-100 spectrometers as well as on a JNM-4H100 spectrometer. The internal standards were tetramethylsilane for the measurements in organic solvent and the sodium salt of 3-(trimethylsilyl)propanesulfonic acid for the measurements in D_2O.

Molecular Weight Determination. The molecular weight of the copolymer was measured by a vapor pressure osmometer (Hitachi Perkin-Elmer model 115) in DMF at 55°.

Results and Discussion

Characterization of Copolymer. An equimolar mixture of OXZ and BPL was polymerized at 40° in DMF. As the reaction proceeded, the solution became viscous. After the reaction the polymer was precipitated from DMF solution with ether and dried *in vacuo*. The polymer was a transparent and gummy material, whose appearance was entirely different from the homopolymers of OXZ and BPL which were both powdery. Also the solubility of copolymer was different from the solubilities of two homopolymers. Poly(BPL) is soluble in $CHCl_3$ and DMF, but insoluble in water, and poly(OXZ) is soluble in water and insoluble in DMF, $CHCl_3$, and CH_3CN. The copolymerization product was soluble in water and DMF, and partly soluble in $CHCl_3$, CH_3OH, and CH_3CN. The difference in solubility behaviors is taken to show the formation of a copolymer but not a mixture of two homopolymers.

The copolymer formation was further confirmed by fractionation, which was carried out by the extraction of aqueous solution of copolymer by $CHCl_3$. The chloroform-soluble part was only 3%, and most of the copolymer remained in the aqueous layer. The ir spectrum of the chloroform-soluble part was almost the same as that of the starting copolymer. Thus it is clear that the copolymerization product does not include poly(BPL), and its composition is homogeneous.

The structure of the copolymer was investigated by nmr and ir spectra. Figure 1 shows the nmr spectra of the copolymer and poly(OXZ) both in D_2O. The spectrum of the copolymer has four peaks at τ 1.93 (1 H), 5.67 (2 H), 6.23 (4 H), and 7.20 (2 H). The peaks at τ 1.93 and 6.23 are reasonably assigned to the protons of N-C*H*O and $CH_2N(CH{=}O)CH_2$ groups, respectively. The peak for the *N*-methylene protons (τ 6.23) appears at a lower field than that of poly(OXZ) (τ 6.45). The other two peaks at τ 5.67 and 7.20 are assigned to the protons of C_2OCH_2– and CH_2CO_2 groups, respectively. Figure 2 shows the spectra of the copolymer and poly(BPL)

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[1] A. Tomalia and D. P. Sheetz, *J. Polym. Sci., Part A-1*, 4, 2253 (1966).

[2] (a) W. Seeliger, *Angew. Chem.*, 78, 613, 913 (1966); (b) T. Kagiya, S. Narisawa, T. Maeda, and K. Fukui, *J. Polym. Sci., Part B*, 4, 441 (1966); (c) T. G. Bassiri, A. Levy, and M. Litt, *ibid.*, 5, 871 (1967).

[3] T. Saegusa, H. Ikeda, and H. Fujii, *Polym. J.*, 3, 35 (1972).

[4] T. Saegusa, H. Ikeda, and H. Fujii, Presented at the 24th Annual Meeting of the Chemical Society of Japan, Osaka, April 3, 1971; manuscript in preparation.

[5] T. L. Gresham, J. E. Jansen, F. W. Shaver, P. A. Bankert, and F. T. Fiedork, J. *J. Amer. Chem. Soc.*, 73, 3168 (1951).

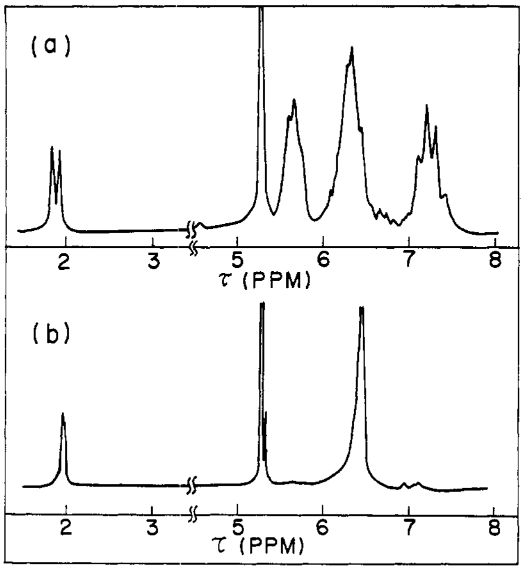


Figure 1. Nmr spectra of (a) OXZ–PBL copolymer, (b) poly(OXZ) in D_2O.

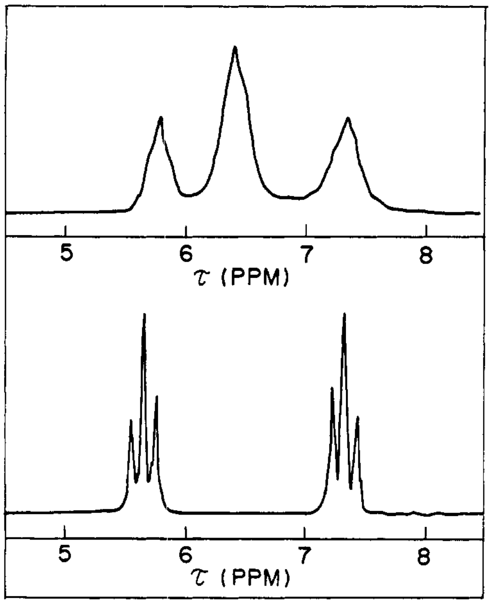


Figure 2. Nmr spectra of (a) OXZ–BPL copolymer, (b) poly(BPL) in a mixture of DMF-d_7 and $CDCl_3$.

in a mixture of DMF-d_7 and $CDCl_3$. In the spectrum of the copolymer, the CO_2CH_2 peak appears at slightly higher field (τ 5.67) in comparison with the corresponding peak of poly(BPL) (τ 5.55). Figures 1 and 2 indicate the formation of copolymer. On the basis of the relative intensities of the peaks at τ 5.67 (BPL unit) and at 6.23 (OXZ unit), the copolymer composition was determined. Thus, the copolymer obtained from an equimolar mixture of OXZ and BPL was found to have 47 mol % OXZ unit.

Figure 3 shows the ir spectra of the copolymer and two homopolymers. The copolymer has characteristic bands at 1740 cm^{-1} due to the CO_2 group and at 1670 cm^{-1} due to the >NHC=O group. The positions of these bands are very close to the corresponding ones of the homopolymers. The other characteristic bands of the copolymer, at 1400, 1170, and 1090–1020 cm^{-1}, are also observed in the spectra of the homopolymers.

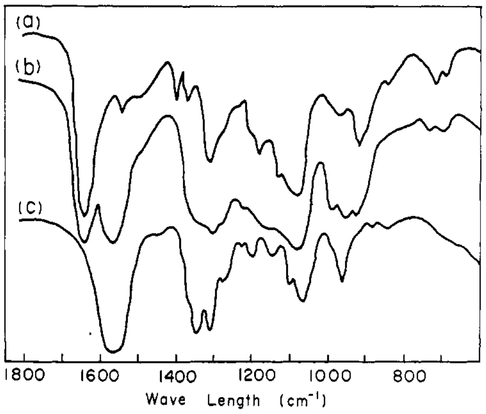
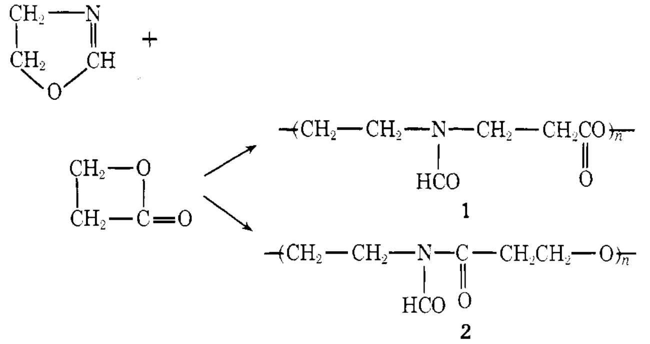


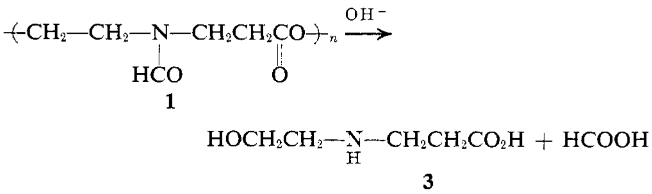
Figure 3. Infrared spectra of (a) poly(BPL) (film), (b) OXZ–BPL copolymer (film), (c) poly(OXZ) (KBr).

As to the modes of linkage between the OXZ and BPL units, the two possibilities **1** and **2** may be considered according to the position of the ring cleavage of BPL. Cleavage

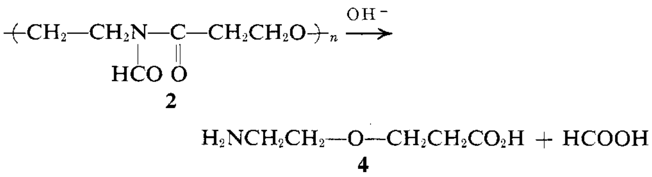


at the CH_2—O bond gives type **1** (amino–ester type) and cleavage at O—C=O bond gives type **2** (amide–ether type). The results of the nmr and ir analyses of the copolymer strongly support structure **1**.

In addition, convincing support for the proposed structure **1** was provided by alkaline hydrolysis of the copolymer at 98°. On alkaline hydrolysis polymers of types **1** and type **2** would respectively give **3** and **4**. The nmr spectrum of the alkaline



$$\underset{\textbf{1}}{\text{-(}CH_2\text{—}CH_2\text{—}\underset{\displaystyle HCO}{N}\text{—}CH_2CH_2\underset{\displaystyle \overset{\|}{O}}{C}O\text{)}_n} \xrightarrow{OH^-} \underset{\textbf{3}}{HOCH_2CH_2\text{—}\underset{H}{N}\text{—}CH_2CH_2CO_2H + HCOOH}$$



$$\underset{\textbf{2}}{\text{-(}CH_2\text{—}CH_2\underset{\displaystyle HCO}{N}\text{—}\underset{\displaystyle \overset{\|}{O}}{C}\text{—}CH_2CH_2O\text{)}_n} \xrightarrow{OH^-} \underset{\textbf{4}}{H_2NCH_2CH_2\text{—}O\text{—}CH_2CH_2CO_2H + HCOOH}$$

hydrolysis product is shown in Figure 4. On the basis of the spectra of the authentic samples of **3** (Na salt) and HCO_2Na, the spectral assignment was made as follows. The singlet at τ 1.60 (1 H) and the triplet at τ 7.34 (4 H) are ascribed to *H*COO and CH_2NCH_2, respectively, and two triplets at τ 6.40 (2 H) and 7.67 (2 H) are assigned to -OCH_2- and -CH_2-CO_2, respectively. On the other hand, the absence of **4** in the hydrolysis product is also indicated by nmr spectral analysis. The nmr spectrum of a reference compound of $CH_3CH_2OCH_2CH_2COOH$ in alkaline D_2O has peaks due to

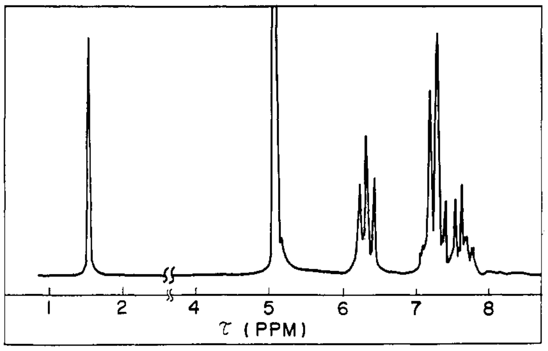


Figure 4. Nmr spectrum of alkaline hydrolysis product of copolymer in D_2O.

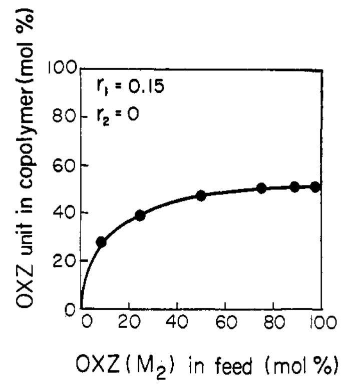


Figure 5. Composition curve of copolymerization of OXZ with BPL (40°, 1 hr, OXZ + BPL = 15 mmol; DMF, 2 ml).

OCH_2CCO_2 and CH_2CO_2 at τ 6.25 and 7.53, respectively. These peaks are not seen in the nmr spectrum of the hydrolysis product of the copolymer.

Furthermore, the presence of long blocks consisting of the same monomer unit in the copolymer was also not observed in the alkaline hydrolysis experiment. The hydrolysis of poly(OXZ) gives crystalline poly(ethylenimine),[6] which is insoluble in water at room temperature. The reaction mixture of alkaline hydrolysis of copolymer was homogeneous and the water-insoluble part was not formed. This finding is taken to support the absence of a long block consisting of OXZ unit.

From the results of the above analyses, it may reasonably be concluded that the copolymer obtained from equimolar amounts of OXZ and BPL consists mainly of the structure of I, *i.e.*, the 1:1 alternating copolymer.

Variation of Copolymerization Conditions. Mixtures of varying compositions of comonomers were polymerized at 40° in DMF. The relation between the composition of monomer mixture and that of the product copolymer is shown in Figure 5. The copolymer composition was determined by nmr. The apparent copolymerization parameters were determined by the curve-fitting method, $\gamma_{BPL} = 0.15$ and $\gamma_{OXZ} = 0$. The values of the monomer reactivity ratio are taken as an indication of the high alternating tendency. Also, they were consistent with the observation that the 1:1 alternating copolymer was formed when the mole fraction of OXZ in the monomer mixture was over 0.50.

The effect of the monomer composition upon the copolymer yield is illustrated in Figure 6. The copolymer yield is the highest at a mole fraction of OXZ of 0.40–0.50. It is of interest to note that the addition of 10 mol % OXZ causes the reaction which consists mostly of the BPL polymerization. This finding is particularly important from the fact that under these milder conditions, *i.e.*, at 40° without any added initiator, the BPL homopolymerization does not take place in the absence of OXZ. A small amount of OXZ is responsible for the initiation.

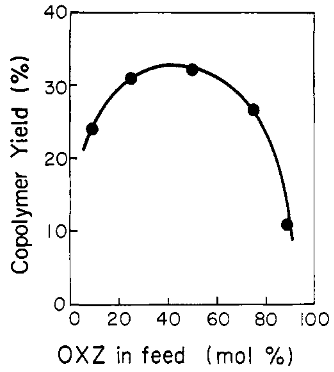


Figure 6. Conversion *vs.* monomer composition in the copolymerization of OXZ with BPL (40°, 1 hr, OXZ + BPL = 15 mmol; DMF, 2 ml).

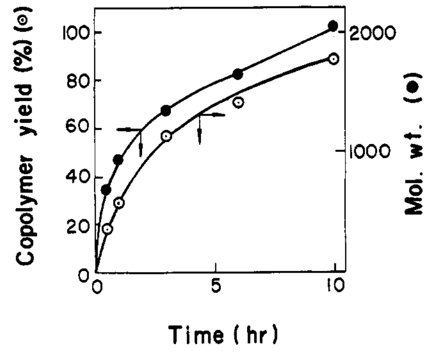


Figure 7. Time–conversion curve of the copolymerization of OXZ with BPL (40°, OXZ = BPL = 7.5 mmol; DMF, 2 ml).

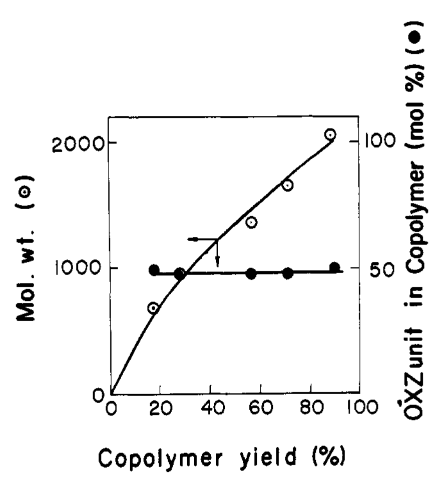


Figure 8. Molecular weight and composition of copolymer *vs.* conversion in the copolymerization of OXZ with BPL (40°, OXZ = BPL = 7.5 mmol; DMF, 2 ml).

Typical examples of the relations between time and conversion and time and molecular weight of copolymer are shown in Figure 7. In this series of experiments, equimolar mixtures of OXZ and BPL were polymerized in DMF at 40°. The reaction is very fast in the early stages of polymerization, and it becomes slower in the later stage. The molecular weight increases as the reaction progresses. Figure 8 shows

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[6] T. Saegusa, H. Ikeda, and H. Fujii, *Macromolecules*, **5**, 359 (1972).

that the molecular weight increase is almost proportional to the conversion percent, and that the copolymer composition remains at about 1 : 1 ratio throughout the polymerization.

The effect of polymerization temperature on the copolymer yield and the copolymer composition is illustrated in Table I.

TABLE I
EFFECT OF TEMPERATURE[a] ON THE COPOLYMERIZATION OF OXZ WITH BPL

Temp, °C	Time, hr	Copolym yield, %	OXZ in copolym, mol %	Copolym mol wt
40	3	70	47	1100
80	2	78	43	2600
120	0.5	80	40	4100

[a] OXZ = BPL = 7.5 mmol; DMF, 2 ml.

The rise of temperature caused a slight decrease of the OXZ content in the copolymer.

Table II shows the effect of solvent. An equimolar mixture of OXZ and BPL was polymerized in various solvents at 40°. The polymer yield is greatly affected by the nature of the solvent. The use of aprotic polar solvents gives higher polymer yields. Especially, the highest polymer yield was obtained by using DMF as the solvent. The copolymer composition, however, was not changed by the nature of solvent.

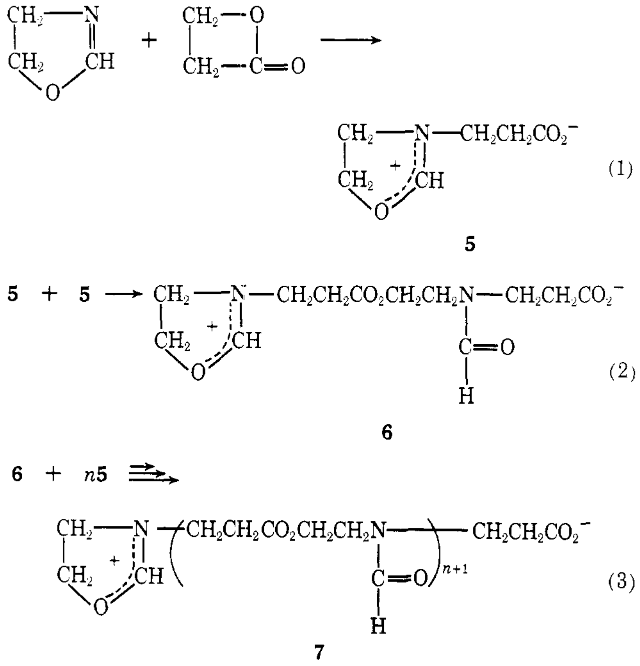
TABLE II
EFFECT OF SOLVENT[a] ON THE COPOLYMERIZATION OF OXZ WITH BPL[b]

Solvent	Copolym yield, %	OXZ in copolym, mol %
DMF	70	47
CH_3CN	39	52
CH_2ClCH_2Cl	26	50
n-Bu_2O	29	45
Toluene	9	46

[a] OXZ = BPL = 3.75 mmol; solvent, 2 ml. [b] 40° for 3 hr.

The copolymerization was carried out in pyridine, and the product was fractionated by liquid–liquid extraction in a $CHCl_3$–H_2O system. The $CHCl_3$-soluble part was poly(BPL) (70%) and the H_2O-soluble part contained the betaine from BPL–pyridine and a very small amount of copolymer. The BPL–pyridine betaine was identified by direct comparison of its nmr spectrum with that of the authentic sample.[4] This result indicates that BPL reacts preferably with pyridine, which is more basic than OXZ, and is polymerized by the so-called anionic mechanism.[7]

Mechanism of Alternating Copolymerization. Several findings described in the preceding section may be compatible with the mechanistic scheme for "the propagation of betaine" shown in eq 1–3. The betaine **5** is first formed from BPL and OXZ (eq 1). Then the reaction of 2 mol of betaine **5** takes place, in which the carboxylate group of one betaine behaves as a nucleophile to attack the *O*-methylene carbon atom of the oxazolinium ring of another betaine to cause the ring-opening isomerization of the oxazolinium ring (eq 2). A dimeric zwitterion of **6** is thus formed, which in turn reacts successively with **5** (eq 3) in the same way as in the reaction of two molecules of **5**. The propagation consists of the successive linkings of betaine molecules to one of ionic ends of the macrozwitterion **7** through the interaction between the carboxylate group and oxazolinium ring. As to the combination of carboxylate and oxazolinium ring, there are two possibilities; *i.e.*, the reaction of the macrozwitterion with the monomeric betaine **5** may occur either at the oxazolinium end or at the carboxylate end of macrozwitterion **7**. This problem has not yet been settled.



The polymerization by the intermediate betaine has been mentioned in the polymerization of a lactone by tertiary amine initiator[7] as well as in the copolymerizations of lactones (β-propiolactone and pivalolactone) with cyclic imines.[8,9] The present study presents an interesting example of alternating copolymerization which consists exclusively of the successive addition of betaine. The formation of oxazolinium ion in the system of the OXZ–BPL copolymerization has been supported by the nmr spectrum of an early reaction mixture of the equimolar copolymerization in CD_3CN which showed a small triplet peak at τ 4.93. This nmr absorption is assigned to the $-O-CH_2-$ protons of the oxazolinium ring of betaine species **5**–**7** on the basis of an nmr spectroscopic studies on the OXZ polymerization by cationic initiators.[10] The above scheme explains the structure of the 1 : 1 alternating copolymer. The successive addition of betaine **5** to the propagating species of a macrozwitterion is supported by the increase of molecular weight of product polymer in parallel with the progress of conversion (Figure 8). The initiation of the BPL polymerization by a small amount of OXZ is rationalized also by assuming the formation of betaine **5**, whose carboxylate group functions as the initiator of the anionic polymerization of BPL.

In the copolymerization, two competitive propagations, the betaine propagation and the anionic propagation of BPL, may possibly occur concurrently. When the mole fraction of OXZ in the comonomer mixture is below 0.5, the fraction of the OXZ unit in the copolymer is below 0.5 (Figure 5). In the copolymerization of the feed ratio in this region, the reaction of BPL with the carboxylate end of the macro-

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(7) V. Jaacks and N. Mathes, *Makromol. Chem.*, **131**, 295 (1970); **142**, 209 (1971).

(8) D. R. Wilson and R. G. Beaman, *J. Polym. Sci., Part A-1*, **8**, 2161 (1970).

(9) T. Kagiya, S. Narisawa, K. Manabe, and K. Fukui, *Kogyo Kagaku Zasshi*, **68**, 1741 (1965); *J. Polym. Sci., Part B*, **3**, 617 (1965).

(10) T. Saegusa, H. Ikeda, and H. Fujii, *Polym. J.*, in press.

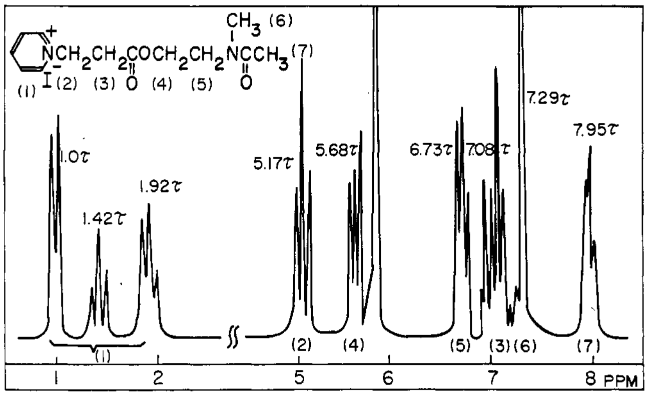


Figure 9. Nmr spectrum of the reaction mixture of betaine **8** and oxazolinium salt **9** in CD_3CN-CD_3OD (4:1) at 40° for 30 min.

TABLE III
COPOLYMERIZATION OF BPL WITH 2-OXAZOLINES[a]

2-Oxazolines	Copolym yield, %	Oxazoline in copolym, mol %
2-Oxazoline	70	47
2-Methyl-2-oxazoline	52	11
2-Phenyl-2-oxazoline	23	4

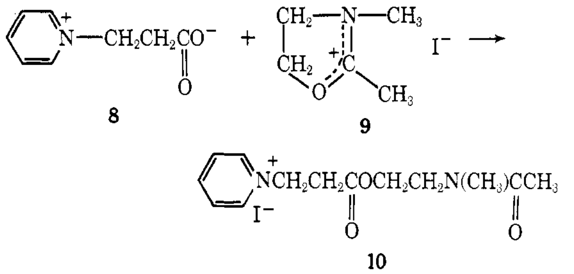
[a] Oxazoline = BPL = 3.8 mmol; DMF, 1-2 ml; 40° for 3 hr.

zwitterion takes place in addition to the regular propagation of **5**. When the mole fraction of OXZ in the comonomer mixture is above 0.5, the betaine propagation proceeds exclusively to produce the 1:1 alternating copolymer. The mole fraction of the OXZ unit in copolymer does not exceed 0.5. At higher temperatures, the BPL units predominate in the copolymer (Table I). This deviation from 1:1 composition may be due to the increase of the relative reactivity of BPL at higher temperatures.

The rate increase of the alternating copolymerization in aprotic polar solvents (Table II) is also explained by the mechanism of betaine propagation. In the above scheme, the formation of betaine **5** may be the rate-determining step. So, the formation of ionic species **5** from two neutral species, OXZ and BPL, is favored in polar solvents.

The effect of pyridine solvent is also taken to support the betaine propagation mechanism. Pyridine is a stronger base than OXZ. Therefore, only the pyridine-BPL betaine is formed, which initiates the homopolymerization of BPL.

The interaction between the oxazolinium ring and the carboxylate group in the above scheme has also been verified by a model reaction (4) in which *N*-methyl-2-methyloxazolinium iodide (**9**) was treated with an equimolar amount of the betaine from pyridine and BPL (**8**). Figure 9 shows the nmr spectrum of the reaction mixture in CD_3CN-CD_3OD at 40° after 30 min. The disappearance of the peak for the $-O-CH_2-$ protons of the oxazolinium ring and the appearance of the peak for the $-OCH_2-$ protons of the ester at τ 5.17 were clearly observed. Analysis of the whole nmr spectrum indicates the formation of **10**, and the ring-opening isomerization of **9** by nucleophilic attack of the carboxylate of **8** is demonstrated.


(4)

Copolymerization of BPL with 2-Substituted 2-Oxazolines. Copolymerizations of BPL with 2-substituted 2-oxazolines were then examined. The 2-substituted 2-oxazolines were 2-methyl-2-oxazoline (MeOXZ) and 2-phenyl-2-oxazoline (PhOXZ). An equimolar mixture of BPL and a 2-substituted 2-oxazoline was heated in DMF at 40° (Table III). Copolymer was obtained, but it was not the 1:1 alternating one, with either MeOXZ or PhOXZ. In these copolymers, the oxazoline unit having the structure of *N*-acylethylenimine was much smaller than 50 mol %.

Under the reaction conditions of the present study, the 1:1 alternating copolymerization with BPL is only possible with unsubstituted 2-oxazoline. In the cases of MeOXZ and PhOXZ, BPL is incorporated in the copolymer not only through the betaine intermediate but also through the anionic ring-opening reaction. This result may be rationalized either by the decreased rate of betaine formation or by the decreased reactivity of 2-substituted oxazolinium ion of the species corresponding to **5-7**. In a previous study by us,[4] it was shown that the ring-opening reactivity of 2-methyloxazolinium ring is much lower than that of the unsubstituted one. Thus, the carboxylate group of betaine and the macrozwitterion attacks not only the oxazolinium ring but also free BPL in the BPL-MeOXZ copolymerization. In the case of PhOXZ, the failure of the 1:1 alternating copolymerization may be ascribed to the decreased rate of betaine formation and, hence, the decreased concentration of betaine. A previous study by us[4] has also shown the decreased nucleophilic reactivity of PhOXZ in comparison with OXZ and MeOXZ. Betaine formation, which is due to nucleophilic attack of an oxazoline component on BPL, will be slow in the case of PhOXZ.