(4) Skolnick, J. *Macromolecules* **1984**, *17*, 645.
(5) Holtzer, M. E.; Holtzer, A.; Skolnick, J. *Macromolecules* **1983**, *16*, 173.
(6) Holtzer, M. E.; Holtzer, A.; Skolnick, J. *Macromolecules* **1983**, *16*, 462.
(7) Lehrer, S. *J. Mol. Biol.* **1978**, *118*, 209.
(8) Woods, E. *Aust. J. Biol. Sci.* **1976**, *29*, 405.
(9) Crimmins, D.; Isom, L.; Holtzer, A. *Comp. Biochem. Physiol. B* **1981**, *69B*, 35.
(10) Potekhin, S.; Privalov, P. *J. Mol. Biol.* **1982**, *159*, 519.
(11) Hodges, R.; Saund, A.; St. Pierre, S.; Reid, R. *J. Biol. Chem.* **1981**, *256*, 1214.
(12) Tsong, T. Y.; Himmelfarb, S.; Harrington, W. F. *J. Mol. Biol.* **1983**, *164*, 431.
(13) Schwarz, G. *Biopolymers* **1968**, *6*, 873.
(14) Zimm, B.; Bragg, J. K. *J. Chem. Phys.* **1959**, *31*, 526.
(15) (a) Vol'kenstein, M. V.; Gotlib, Y.; Ptitsyn, O. B. *Fiz. Tverdogo Tela* **1961**, *3*, 420. (b) Gotlib, Y. Y. *Fiz. Tverdogo Tela* **1961**, *3*, 2170.
(16) Go, N. *J. Phys. Soc. Jpn.* **1967**, *22*, 416.
(17) Craig, M. E.; Crothers, D. M. *Biopolymers* **1968**, *6*, 385.
(18) Rawlings, P. K.; Schneider, F. W. *Ber. Bunsenges. Phys. Chem.* **1973**, *77*, 237.
(19) Chay, T. R.; Stevens, C. L. *Macromolecules* **1975**, *8*, 531.
(20) Silberberg, A.; Simha, R. *Biopolymers* **1968**, *6*, 479.
(21) Rabinowitz, P.; Silberberg, A.; Simha, R.; Loftus, E. *Adv. Chem. Phys.* **1969**, *15*, 281.
(22) Simha, R.; Silberberg, A. *Macromolecules* **1972**, *5*, 332.
(23) Schwarz, G. *J. Mol. Biol.* **1965**, *11*, 64.
(24) Poland, D.; Scheraga, H. A. *J. Chem. Phys.* **1966**, *45*, 2071.
(25) Craig, M. E.; Crothers, D. M. *Biopolymers* **1968**, *6*, 385.
(26) Lumry, R.; Legare, R.; Miller, W. G. *Biopolymers* **1964**, *2*, 486.
(27) Barksdale, A.; Stuehr, J. *J. Am. Chem. Soc.* **1972**, *94*, 3334.
(28) Zana, R.; Lang, J. *Biopolymers* **1973**, *12*, 79.
(29) Schwarz, G.; Seelig, J. *Biopolymers* **1968**, *6*, 1263.
(30) Wada, A.; Tanaka, T.; Kihara, H. *Biopolymers* **1972**, *11*, 587.
(31) Tanaka, T.; Wada, A.; Suzuki, M. *J. Chem. Phys.* **1973**, *59*, 3799.
(32) Ishiwari, K.; Nakajima, A. *Macromolecules* **1978**, *11*, 785 and references cited therein.
(33) Chay, T. R.; Stevens, C. L. *Biopolymers* **1973**, *12*, 2563.
(34) Miller, W. G. *Macromolecules* **1973**, *6*, 100.
(35) (a) Jernigan, R. L.; Ferretti, J. A.; Weiss, G. H. *Macromolecules* **1973**, *6*, 684. (b) Jernigan, R. L.; Ferretti, J. A. *J. Chem. Phys.* **1975**, *62*, 2519.
(36) McQuarrie, D. A.; McTague, J. P.; Reiss, H. *Biopolymers* **1965**, *3*, 657.
(37) McLachlan, A.; Stuart, M. *J. Mol. Biol.* **1975**, *98*, 293.
(38) Stone, D.; Smillie, L. *J. Biol. Chem.* **1978**, *253*, 1137.
(39) Mak, A.; Lewis, W.; Smillie, L. *FEBS Lett.* **1979**, *105*, 232.
(40) Glauber, R. J. *J. Math. Phys.* **1963**, *4*, 294.
(41) Poland, D.; Scheraga, H. "Theory of Helix–Coil Transitions in Biopolymers"; Academic Press: New York, 1970.
(42) Morse, P. M.; Feshbach, H. "Methods of Theoretical Physics"; McGraw-Hill: New York, 1953; p 133.
(43) Abramowitz, M.; Stegun, I. A. "Handbook of Mathematical Functions"; Dover: New York, 1972; Chapter 9.
(44) Skolnick, J. *Macromolecules* **1984**, *17*, 2153.
(45) Byron, F.; Fuller, R. "Mathematics of Classical and Quantum Physics"; Addison-Wesley: Reading, MA, 1969; Vol. I.

Polylactones. 1. Copolymerization of Glycolide and ϵ-Caprolactone

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ABSTRACT: Copolymerization of glycolide and ϵ-caprolactone was conducted in bulk at 100 °C and in nitrobenzene or dioxane at 70, 100, or 150 °C. The resulting copolyesters were characterized with respect to their molar composition by means of ^{1}H NMR spectra and with respect to their sequences by means of ^{13}C NMR spectra. The results allow a classification of both copolyesters and initiators. Cationic initiators such as ferric chloride, boron trifluoride, and fluorosulfonic acid favor the incorporation of ϵ-caprolactone, catalyze intermolecular transesterifications, and cause rapid degradation of the polyesters above 100 °C. Complexing catalysts such as zinc chloride, aluminum isopropylate, and dibutyltin dimethylate favor the incorporation of glycolide and chemical heterogeneity of first order. Furthermore, intramolecular transesterification was detected in the case of aluminum isopropylate and dibutyltin dimethylate. Anionic catalysts such as tetramethylammonium benzoate and benzyltriphenylphosphonium chloride only initiate the homopolymerization of glycolide. The polymerization mechanisms are discussed. The differential scanning calorimetry shows a close relationship between crystallinity and nature of sequences.

Introduction

Poly(glycolide) and copolymers of glycolide and LL-lactide have attracted much interest because of their usefulness in medicine, in particular as surgical sutures.[1-3] In addition to satisfactory mechanical properties these copolyesters have a low immunogeneity and an extremely low toxicity. Since interest in biodegradable polymers of low toxicity seems likely to increase in the future, copolyesters other than glycolide and lactide need to be investigated. Hydroxycaproic acid is another building block of relatively low toxicity and a suitable monomer is technically available in the form of ϵ-caprolactone. Poly(ϵ-caprolactone) and copolyesters of ϵ-caprolactone and D,L-lactide have been investigated, especially in regard to biodegradability and for use in drug delivery systems.[4-7] Copolyesters built up of ϵ-caprolactone and glycolyl units are interesting because they allow a broad variation of their chemical and physical properties. Poly(glycolide) is a rigid, highly crystalline material with a melting point around 219 °C. It is insoluble in most organic solvents, including trifluoroacetic acid, and a has high crystal density (1.7 g/cm^3). Poly(ϵ-caprolactone) is a more flexible material which has a low melting point (56 °C), a low crystal density (1.2 g/cm^3), and good solubility in most organic solvents. To the best of our knowledge, copolyesters of glycolide and ϵ-caprolactone were never studied in detail. Thus, it was the purpose of the present paper to investigate various copolymerizations of glycolide and ϵ-caprolactone, to characterize the sequences by means of NMR spectroscopy, and to relate the sequence to the reaction mechanisms, on the one hand, and to properties, such as solubility and crystallinity, on the other hand.

Experimental Section

Monomers. ϵ-Caprolactone (EGA-Chemie, D-7924 Steinheim) was distilled under nitrogen over oligomeric 4,4′-diisocyanatodiphenylmethane. Glycolide was prepared by thermal condensation of sodium chloroacetate in the presence of copper turnings.[8] It was washed with diethyl ether and recrystallized from dry

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ethanol (mp 82–83 °C in agreement with ref 8).

Initiators. Dry zinc chloride, ferric chloride, aluminum chloride, boron trifluoride etherate, and fluorosulfonic acid were used as purchased from Merck & Co. (D-6100 Darmstadt). Aluminum isopropylate was prepared from aluminum and dry 2-propanol by means of mercury chloride. It was distilled in vacuo before use. Dibutyltin dimethylate was prepared from dibutyltin dichloride and sodium methoxide in dry methanol. It was distilled once in vacuo before use.

Copolymerizations. The mixture of 1.94 g (30 mmol) of glycolide and 6.78 g (60 mmol) of ϵ-caprolactone was heated to 100 °C to obtain a homogeneous melt of both monomers. This mixture was then either polymerized in bulk by direct addition of 0.9 mmol of a suitable initiator or diluted with 20 mL of dry nitrobenzene (distilled over P_4O_{10}). Before the copolymerizations were started, the reaction vessels were silanized by means of dimethyldichlorosilane. The reaction vessels (Erlenmeyer flasks with ground joints) were closed with glass stoppers and steel springs and completely immersed into the heating bath to prevent selective distillation of one monomer to colder parts of the reaction vessel. When the reaction time was over, the reaction product was dissolved in 50 mL of a mixture of methylene chloride and trifluoroacetic acid (1:1 by volume) and precipitated into 600 mL of cold methanol. The precipitated copolyesters were filtered off and dried at 50 °C (12 mbar) and 60 °C (10^{-2} mbar).

Transesterifications. Homogeneous solutions of 30 mmol of glycolide and 30 mmol of poly(ϵ-caprolactone) ($\overline{DP} > 100$) in 15 mL of dry nitrobenzene were prepared by heating the components under shaking to 100 °C for several minutes. Then a catalyst (0.5 mmol) was added, and the reaction mixtures were allowed to react and then worked up as described for the copolymerization.

Fractionations. The copolyesters (5-g samples) were stirred in 50 mL of dry dimethylformamide for 30 min at 100 °C. Then the hot suspensions were filtered through a glass frit. The filter cake was washed with cold methanol and the filtrate was precipitated into 400 mL of cold methanol. The isolated fractions were dried at 50 °C (12 mbar) and 60 °C (10^{-2} mbar).

NMR Measurements. Solutions of 10 wt % copolyester in pure trifluoroacetic acid (TFA) were measured on a Bruker WH 90 FT NMR spectrometer (2.3-T magnet) at 28–30 °C. The ^1H NMR measurements were conducted in 5-mm-o.d. sample tubes with internal Me_4Si as shift reference. The ^{13}C NMR measurements were conducted in 10-mm-o.d. sample tubes with a coaxial 4-mm tube containing a 1:1 mixture of dioxane-d_8 and Me_4Si for lock purposes and shift referencing. The following acquisition parameters were used: pulse width 4 μs (ca. 30°), 8K data points/5000 Hz spectral width zerofilled to 16K before Fourier transform, exponential line broadening 1 Hz (ca. 10 000–40 000 transients). Under these conditions a slight saturation of the CO signals was observed. However, the intensity ratios used in eq 1 and 2 did not change when the repetition time was increased.

DSC Measurements. Samples of 2–3 mg (weighed into aluminum pans) were measured on a Perkin-Elmer DSC-2 at a heating rate of 20 °C/min.

Results and Discussion

NMR Sequence Analysis. In previous papers dealing with the synthesis and spectroscopic characterization of aliphatic copolyamides[9–14] we have shown that sequence analyses are best attained by means of ^{13}C NMR spectroscopy. ^1H NMR spectra up to 400 MHz are not sensitive to sequence effects, whereas ^{15}N NMR spectra are in many cases difficult to interpret.[10] It is characteristic for the ^{13}C NMR spectra of copolyamides that the CO signals are most sensitive to sequence effects followed the $N-CH_2$ groups, whereas carbons in other positions normally do not provide sequence information. Similar spectroscopic properties were found for copolyesters prepared from diacids and diols. The CO signals are more sensitive to sequence effects than $O-CH_2$ signals.[15,16] Signals of other carbons are rather insensitive and the usefulness of ^1H NMR spectra is restricted to a special class of poly(terephthalates).[17]

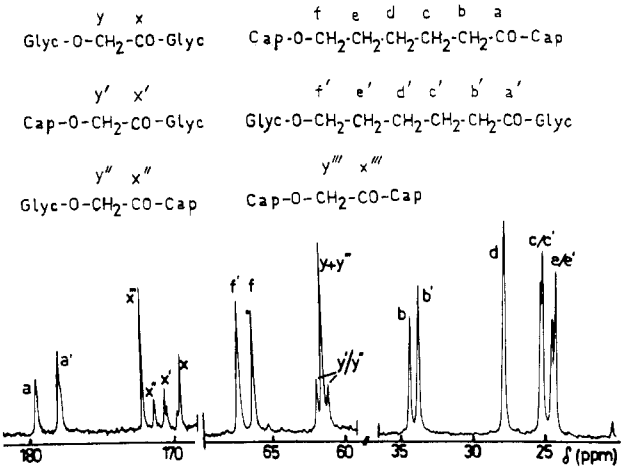
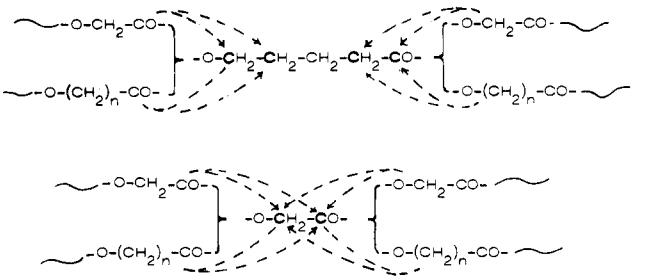


Figure 1. 22.63-MHz ^{13}C NMR spectrum of the copolyester no. 3, Table IV, measured in TFA.

Scheme I
Influence of Dyad and Triad Sequences on the ^{13}C NMR Signals of Glycolyl and ϵ-Hydroxycaproyl Units



The ^1H and ^{13}C NMR spectra of our glycolide/ϵ-caprolactone copolyesters fit well into this picture. The ^1H NMR spectra up to 270 MHz do not give sequence information but they were useful in determining the mole ratios of both kinds of monomer units in the isolated copolyesters (Glyc/Cap ratios in Tables I and II). Furthermore, the ^1H NMR spectra allowed the identification of alkyl ester end groups. The sequence analyses were performed by means of ^{13}C NMR spectra, and, as expected, the CO signals proved to be most sensitive to sequence effects. Scheme I demonstrates the nature of the sequence effects as observed for 22.63-MHz spectra. The α-, β-, δ-, and ϵ-carbons of ϵ-hydroxycaproyl units experience a dyad effect, whereas both carbons of the glycolyl units exhibit a triad sensitivity. In most spectra we even observed a triad sensitivity of the CO signals of the ϵ-hydroxycaproyl units and a tetrad sensitivity of the glycoyl units. However, because we were not able to reliably assign the individual peaks of this fine structure we restricted our sequence analysis to the dyad and triad effects outlined in Scheme I.

The assignments of the dyad and triad peaks presented in Figure 1 were obtained in the following way. The peaks of the homogeneous bonds were assigned by addition of poly(ϵ-caprolactone) and oligo(glycolide) to solutions of copolyesters. This simple measure suffices to assign all dyad peaks of the ϵ-caprolactone units. The triad peaks of the glycolyl units were assigned on the basis of the following chemical and spectroscopic considerations. For a true copolymerization the rates of the two crossover steps must be identical (eq 1), and thus, the peak intensities I_{GGC} and I_{GGG} must also be identical. The peaks x′ and x″ as well as y′ and y″ met these requirements. Furthermore, the extent of transesterification should increase with increasing temperature and reaction time when cationic

Table I
Copolymerizations of Glycolide and ε-Caprolactone in Bulk at 100 °C by means of Acidic Initiators

no.	initiator[a]	Glyc/Cap[b]	time, h	yield,[c] %	Glyc/Cap[d]	av block lengths $\bar{L}_G$	av block lengths $\bar{L}_C$
1	$FeCl_3$	1.0	8	75.5	0.96	2.8	2.9
2	$FeCl_3$	1.0	44	55.5	0.92	2.6	2.8
3	$FeCl_3$	1.0	120	0.0			
4	$AlCl_3$	1.0	8	1.0			
5	$AlCl_3$	1.0	44	31.5	7.72	17.0	2.2
6	$BF_3{\cdot}Et_2O$	1.0	0.25	38.5	0.13	3.0	23.0
7	$BF_3{\cdot}Et_2O$	1.0	0.5	45.5	0.16	3.1	19.0
8	$BF_3{\cdot}Et_2O$	1.0	2	62.0	0.33	4.0	12.0
9	$BF_3{\cdot}Et_2O$	1.0	8	83.5	0.93	8.7	9.5
10	$BF_3{\cdot}Et_2O$	1.0	16	84.0	0.95	8.8	9.5
11	$BF_3{\cdot}Et_2O$	1.0	30	89.0	0.98	9.0	9.3
12	$BF_3{\cdot}Et_2O$	1.0	44	91.0	0.97	9.0	9.2
13	FSO_3H	1.0	0.25	0.5			
14	FSO_3H	1.0	0.5	15.0	0.17	2.0	11.7
15	FSO_3H	1.0	2	38.0	0.23	2.1	10.3
16	FSO_3H	1.0	8	42.0	0.26	2.2	9.5
17	FSO_3H	1.0	16	43.5	0.27	2.2	9.3
18	FSO_3H	1.0	30	46.5	0.29	2.3	8.7
19	FSO_3H	1.0	44	58.5	0.33	2.4	7.3

[a] Mole ratio initiator/sum of both monomers = 1:100. [b] Feed ratio glycolyl/hydroxycaproyl units, i.e., glycolide/caprolactone = 1:2. [c] After precipitation from methanol. [d] Mole ratio of glycolyl/hydroxycaproyl units in the isolated copolyesters (from ^1H NMR spectra).

Table II
Copolymerizations of Glycolide and ε-Caprolactone in Nitrobenzene by means of Acidic Initiators

no.	initiator[a]	Glyc/Cap[b]	temp, °C	time, h	yield,[c] %	Glyc/Cap[d]	av block lengths $\bar{L}_G$	av block lengths $\bar{L}_C$
1	$FeCl_3$	1.0	70	44	60.5	0.98	2.9	2.9
2	$FeCl_2$	1.0	100	44	61.0	1.17	3.2	2.8
3	$AlCl_3$	1.0	100	2.5	1.0			
4	$AlCl_3$	1.0	100	44	23.5	0.07	<4.0	>30.0
5	$BF_3{\cdot}Et_2O$	1.0	70	44	77.5	0.53	7.0	13.0
6	$BF_3{\cdot}Et_2O$	1.0	100	2.5	54.5	0.18	4.0	21.0
7	$BF_3{\cdot}Et_2O$	1.0	100	44	87.5	0.97	10.6	11.0
8	$BF_3{\cdot}Et_2O$	1.0	150	44	35.0	1.12	3.2	2.8
9	FSO_3H	1.0	70	44	2.6			
10	FSO_3H	1.0	100	2.5	0.0			
11	FSO_3H	1.0	100	44	27.9	0.05	2.0	50.0
12	FSO_3H	1.0	150	44	71.7	0.60	2.9	5.0

[a] Mole ratio initiator/sum of both monomers = 1:100. [b] Feed ratio glycolyl/hydroxycaproyl units, i.e., glycolide/caprolactone = 1:2. [c] After precipitation from methanol. [d] Mole ratio of glycolyl/hydroxycaproyl units in the isolated copolyesters.

catalysts such as FSO_3H or $FeCl_3$ were used. In agreement with this expectation the intensity of peak x‴, which is attributed to the sequence C–G–C, grew with increasing temperature and reaction time (Figure 2). The spectroscopic arguments in favor of our assignments concern the consistency of the observed shift effects. Provided the assignments of x′ and x″ are correct, peak x‴ must absorb furthest downfield from x, because the downfield shifts which the C units exert on the central G unit in the triads C–G–G and G–G–C are combined in the sequence C–G–C. The differentiation between x′ and x″ is based on the consideration that the C unit attached to the carboxyl group of a G unit presumably causes a stronger downfield shift than the C unit bound to the OH group. In the case of the CH_2 signal, the peak y′ and y″ were attributed to the triads C–G–G and G–G–G because of their equal intensities. Since the shift effects which the C units exert on the central G unit in these two triads are opposite, they must cancel each other in the triad C–G–C. Hence, nearly identical chemical shifts are expected for the CH_2 peaks of the triads C–G–C and G–G–G, and the CH_2 peaks of these two triads were not resolved in our 22.63-MHz spectra.

Two kinds of information were extracted from the ^{13}C NMR spectra, namely the average lengths of the homogeneous blocks (I_G and I_C in Tables I–VI) and the presence

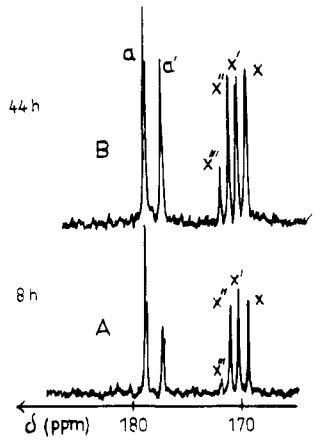


Figure 2. Carbonyl signals in the 22.63-MHz ^{13}C NMR spectra of the copolyester no. 16, Table I (A), and no. 19, Table I (B).

of the sequence C–G–C (C = caprolactone, G = glycolyl units). The average lengths of the caprolactone blocks ($\bar{L}_C$) were calculated from the dyad peaks of the CO or OCH_2 signals according to eq 2.

$$V_{CGG} = V_{GGC} = k_{CGG}[\sim C][G] = k_{GGC}[\sim G][C] \quad (1)$$

$$\bar{L}_C = I_{CC}/I_{CG} + 1 = I_{CC}/I_{GC} + 1 \quad (2)$$

Table III
Copolymerizations of Glycolide and ε-Caprolactone in Bulk at 100 °C by means of Complexing Initiators

no.	initiator[a]	Glyc/Cap[b]	time, h	yield,[c] %	Glyc/Cap[d]	av block lengths $\bar{L}_G$	av block lengths $\bar{L}_C$
1	$ZnCl_2$	1.0	8	4.0	∞	∞	
2	$ZnCl_2$	1.0	44	45.5	4.4	11.9	2.7
3	$Al(O\text{-}i\text{-}Pr)_3$	1.0	0.5	17.5	17.5	24.5	1.4
4	$Al(O\text{-}i\text{-}Pr)_3$	1.0	2.0	25.0	5.7	14.0	2.5
5	$Al(O\text{-}i\text{-}Pr)_3$	1.0	4.0	42.0	3.5	11.0	3.3
6	$Al(O\text{-}i\text{-}Pr)_3$	1.0	8.0	54.5	2.2	8.5	4.0
7	$Al(O\text{-}i\text{-}Pr)_3$	1.0	16.0	71.5	1.1	6.5	4.5
8	$Al(O\text{-}i\text{-}Pr)_3$	1.0	44.0	80.5	1.04	5.0	4.8
9	$(n\text{-}Bu)_2Sn(OMe)_2$	1.0	2.0	48.0	1.10	2.1	1.9
10	$(n\text{-}Bu)_2Sn(OMe)_2$	1.0	4.0	48.0	1.07	1.9	1.8
11	$(n\text{-}Bu)_2Sn(OMe)_2$	1.0	8.0	52.0	1.02	1.6	1.6
12	$(n\text{-}Bu)_2Sn(OMe)_2$	1.0	44.0	99.0	0.87	1.5	1.8

[a] Mole ratio initiator/sum of both monomers = 1:100. [b] Feed ratio glycolyl/hydroxycaproyl units, i.e., glycolide/caprolactone = 1:2. [c] After precipitation from methanol. [d] Mole ratio glycolyl/hydroxycaproyl units in the isolated copolyesters (from ^1H NMR spectra).

Table IV
Copolymerizations of Glycolide and ε-Caprolactone in Solution by means of Anionic or Complexing Catalysts (Reaction Time = 44 h)

no.	initiator[a]	solvent	Glyc/Cap[b]	temp, °C	yield,[c] %	Glyc/Cap[d]	av block lengths $\bar{L}_G$	av block lengths $\bar{L}_G$
1	$Al(O\text{-}i\text{-}Pr)_3$	nitrobenzene	1.0	70				
2	$Al(O\text{-}i\text{-}Pr)_3$	nitrobenzene	1.0	100	64.5	1.28	3.7	2.9
3	$Al(O\text{-}i\text{-}Pr)_3$	nitrobenzene	1.0	150	50.5	0.93	1.7	1.8
4	$(n\text{-}Bu)_2Sn(OMe)_2$	nitrobenzene	1.0	70	35.0	2.19	5.0	2.2
5	$(n\text{-}Bu)_2Sn(OMe)_2$	nitrobenzene	1.0	100	65.0	0.93	1.8	1.9
6	$(n\text{-}Bu)_2Sn(OMe)_2$	nitrobenzene	1.0	150	0			
7	$(n\text{-}Bu)_2Sn(OMe)_2$	dioxane	1.0	100	53.0	0.85	1.5	1.8
8	$Phe_3P^+\text{-}Bzl\cdot Cl^-$	nitrobenzene	1.0	100	(36.0)[e]	∞	∞	0
9	$Phe_3P^+\text{-}Bzl\cdot Cl^-$	dioxane	1.0	100	(33.0)[e]	∞	∞	0
10	Et_4N^+-benzoate	nitrobenzene	1.0	100	(34.0)[e]	∞	∞	0
11	Et_4N^+-benzoate	dioxane	1.0	100	(35.0)[e]	∞	∞	0

[a] Mole ratio initiator/sum of both monomers = 1:100. [b] Feed ratio glycolyl/hydroxycaproyl units, i.e., glycolide/caprolactone = 1:2. [c] After precipitation from methanol. [d] Mole ratio glycolyl/hydroxycaproyl units in the isolated copolyesters (from ^1H NMR spectra).

Table V
Polymerizations of Glycolide in Nitrobenzene in the Presence of Poly(ε-caprolactone)

no.	initiator	temp, °C	time, h	yield,[a] %	Glyc/Cap[b]	transesterification,[c] %
1	$FeCl_3$	70	44	66.5	1.23	23.5
2	$FeCl_3$	100	44	60.0	1.34	31.0
3	$BF_3\cdot Et_2O$	70	44	87.0	0.48	0.0
4	$BF_3\cdot Et_2O$	100	2	70.0	0.30	3.0
5	$BF_3\cdot Et_2O$	100	44	83.5	1.13	12.0
6	$BF_3\cdot Et_2O$	150	44	30.0	1.10	84.0
7	FSO_3H	70	44	79.5	0.52	0.0
8	FSO_3H	100	2	63.0	0.30	0.0
9	FSO_3H	100	44	77.0	0.60	9.0
10	FSO_3H	150	44	75.5	0.95	32.5
11	$ZnCl_2$	100	44	72.5	0.25	0.0
12	$AlCl_3$	100	44	68.0	0.40	0.0
13	$Al(O\text{-}i\text{-}Pr)_3$	100	44	87.5	0.84	0.0
14	$Al(O\text{-}i\text{-}Pr)_3$	150	44	72.0	0.84	0.0
15	$(n\text{-}Bu)_2Sn(OMe)_2$	150	44	95.0	0.81	0.0
16	$(n\text{-}Bu)_2Sn(OMe)_2$	150	44	21.0	∞	0.0

[a] Referred to $I_{CG}/I_{CC} \times 100$ sum of poly(glycolide) and poly(ε-caprolactone). [b] Mole ratio glycolyl/hydroxycaproyl units of the precipitated (co)polyesters. [c] Intensity ratios $I_{CG}/I_{CC} \times 100$ from the ^{13}C NMR spectra of the precipitated (co)polymers.

I_{CC} is the intensity of a peak representing the C–C dyad (a or f in Figure 1), and I_{CG} is the intensity of a peak representing the C–G dyad (a′ or f′ in Figure 1).

$$\bar{L}_G = \frac{I_{GGG} + I_{CGG}}{I_{GGC} + I_{CGC}} + 1 = \frac{I_{GGG} + I_{GGC}}{I_{CGG} + I_{CGC}} \quad (3)$$

I_{GGS} is the intensity of the peak representing the G–G–G sequence (x′ in Figure 1), and I_{GGC} and I_{CGG} are the intensities of the peaks representing triads of two glycolyl and one caprolactone unit (x′ or x″ in Figure 1) I_{CGC} is the intensity of the peak representing the C–G–C triad (x‴ in Figure 1).

$$\frac{\text{Glyc}}{\text{Cap}}\ (^1H\ \text{NMR}) = \frac{\bar{L}_G}{\bar{L}_C}\ (^{13}C\ \text{NMR}) \quad (4)$$

The average lengths of the glycolyl blocks ($\bar{L}_G$) were calculated from the triad peaks of the CO signal according to eq 3. As shown by eq 4, the $\bar{L}_G/\bar{L}_C$ ratio is identical with

Table VI
Fractionation of Copolyesters Prepared from Glycolide and ϵ-Caprolactone in Bulk at 100 °C (Reaction Time = 44 h)

no.	initiator[a]	Glyc/Cap[b]	yield,[c] %	Glyc/Cap[d]	av block lengths		soluble in DMF[e]		insoluble in DMF[e]	
					L_{GG}	L_{CC}	yield, %	Glyc/Cap	yield, %	Glyc/Cap
1	$FeCl_3$	2.0	74.1	1.80	4.1	2.3	81.5	2.00		
2	$FeCl_3$	1.0	55.7	0.95	3.0	3.2	60.0	0.95		
3	$AlCl_3$	2.0	18.0	9.80	28.7	2.9	10.0	4.25	65.5	18.00
4	$AlCl_3$	1.0	31.5	7.70	17.0	2.2	14.5	4.90	66.0	11.70
5	BF_3·Et_2O	2.0	87.0	1.90		1.8	93.5	1.90		
6	BF_3·Et_2O	1.0	91.5	1.00		2.7	92.5	0.95		
7	FSO_3H	2.0	24.5	0.70	9.3	4.9	81.5	0.60		
8	FSO_3H	1.0	58.5	0.35	9.0	9.2	50.0	0.25		
9	$ZnCl_2$	2.0	12.5	14.00	25.2	1.8	1.0	9.0	22.5	24.60
10	$ZnCl_2$	1.0	46.0	4.40	12.0	2.7	33.5	3.50	55.0	5.80
11	$Al(O\text{-}i\text{-}Pr)_3$	2.0	46.0	7.80	18.7	2.4	25.5	1.80	63.5	23.70
13	$Al(O\text{-}i\text{-}Pr)_3$	1.0	80.5	1.10	4.8	4.4	54.0	0.35	35.0	4.50

[a] Mole ratio initiator/sum of both monomers = 1:100. [b] Feed ratio glycolyl/hydroxycaproyl units, i.e., glycolide/caprolactone = 1:2. [c] After precipitation from methanol. [d] Mole ratio glycolyl/hydroxycaproyl units in the isolated copolyesters (from ^1H NMR spectra). [e] Dimethylformamide.

the molar composition of the copolyesters which was determined from ^1H NMR spectra, so that quantification of ^1H NMR signals enables one to check the correctness of ^{13}C NMR signal intensities. It is noteworthy that the sequence analyses obtained from the ^{13}C NMR spectra do not give any information on the chemical heterogeneity of first or second order, unless the NMR measurements were combined with a fractionation of the copolyesters. An investigation in this direction is presented (and discussed) in Table V. Information on the presence of the sequence C–G–C is highly interesting because a simple ring opening of glycolide can never yield this sequence. Hence this sequence indicates that the polymerization was accompanied by transesterification.

Copolymerizations. Four series of copolymerizations were conducted, namely, bulk polymerizations with cationic initiators (Table I), cationic polymerizations in nitrobenzene solution (Table II), bulk polymerizations with complexing initiators (Table III), and polymerizations with anionic or complexing initiators in solution (Table IV). The arguments for the subdivision of the initiators are discussed below. All these copolymerizations were conducted with a glycolide/ϵ-caprolactone mol ratio of 1:2 corresponding to an 1:1 mol ratio of glycolyl and hydroxycaproyl units. For comparison, a few copolymerizations were carried out with glycolide/ϵ-caprolactone ratios of 1:1 (Table V). The standard reaction temperature for the bulk polymerizations of 100 °C was chosen because the high melting point of glycolide prevents a lower temperature and because higher temperatures favor side reactions.

When the copolymerizations summarized in Table I are compared with one another, a similar behavior is detectable for $AlCl_3$, BF_3, and FSO_3H in that the yields of copolyesters increase with the reaction time. The opposite result is found for $FeCl_3$ (nos. 1–3), indicating that this initiator is so reactive that the fast polymerization is immediately followed by degradation of the polyester. This interpretation was confirmed by heating a sample of poly(caprolactone) with $FeCl_3$ at 100 °C for 120 h. After this time no poly(ϵ-caprolactone) precipitated from methanol. Because neither high molecular weight polyester nor monomers were the main products, obviously cyclic oligomers and oligomers with chlorine end groups were predominantly formed. However, $FeCl_3$, BF_3, and FSO_3H behave similarly in that ϵ-caprolactone is preferentially incorporated into the copolyester. This result agrees well with a cationic polymerization mechanism (discussed below) because the ester group of ϵ-caprolactone is more basic than that of glycolide. The copolymerizations initiated with BF_3 and FSO_3H demonstrate, furthermore, that the glycolyl/hydroxycaproyl ratio continuously increases with increasing conversion (nos. 6–19, Table I). Aluminum chloride behaves like all other cationic initiators when the copolymerization is conducted in nitrobenzene (no. 4, Table II). However, in bulk the incorporation of glycolide is favored (no. 5, Table I), suggesting that the mechanism of the $AlCl_3$-initiated polymerization depends on the solvation of the active species.

Except in the case of aluminum chloride the results obtained in nitrobenzene solution agree well with those of the bulk polymerizations. ϵ-Caprolactone is more rapidly incorporated than glycolide and at 100 °C the Glyc/Cap ratio increases with the conversion (nos. 6, 7, 10, and 11, Table II). In two cases (nos. 2 and 8, Table II) the Glyc/Cap ratio is 1.0. However, these Glyc/Cap ratios obtained with $FeCl_3$ at 100 °C and with BF_3 at 150 °C, reaction conditions which favor transesterification and degradation reactions. If ϵ-caprolactone is the more reactive comonomer in the cationic copolymerization, poly(ϵ-caprolactone) is likely to be the more reactive polymer in cationic degradation. Thus, a more rapid degradation of poly(ϵ-caprolactone) blocks in the copolyester must result in a higher Glyc/Cap ratio.

When the average block lengths (calculated according to eq 2) are compared, the following interesting results are obtained. Ferric chloride yields nearly random sequences regardless whether the copolymerization is carried out in bulk (nos. 1 and 2, Table I) or in solution (nos. 1 and 2, Table II). For an entirely random sequence $\bar{L}_G$ and $\bar{L}_C$ values of 2.0 are expected. However, $\bar{L}_G$ and $\bar{L}_C$ values around 3 are expected for copolymerizations of glycolide in the absence of fast transesterification because glycolide is a dimer. The other three initiators yielded copolyesters with blocky sequences. In agreement with the low Glyc/Cap ratios, short Glyc blocks and long Cap blocks are the result of low conversions (nos. 6–8, Table I) and nos. 4, 6, and 11, Table II). With increasing conversion the block lengths of Glyc and Cap units become similar (nos. 9–11, Table I, and nos. 7 and 12, Table II). Thus, the cationic copolymerizations of glycolide and ϵ-caprolactone enable one to synthesize three kinds of copolyesters: (A) copolyesters with a molar composition near 1:1 and a nearly random sequence, (B) copolyesters with a molar composition near 1:1 and a blocky sequence ($\bar{L}_G$ and $\bar{L}_C \sim 10$), and (C) copolyesters with a low Glyc/Cap ratio and long blocks ($\bar{L}_C$ = 20–50) of Cap units.

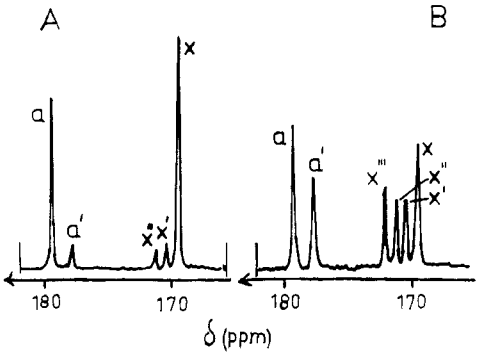


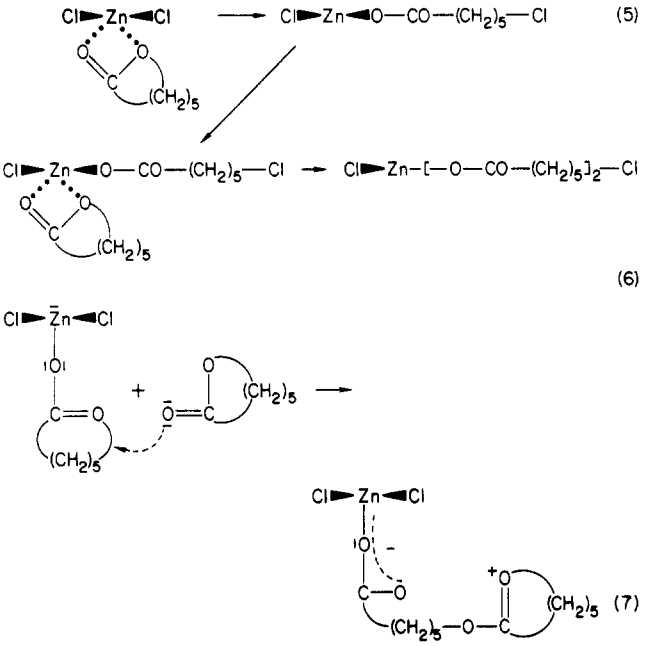
Figure 3. Carbonyl signals in the 22.63-MHz ^{13}C NMR spectra of the copolyesters no. 5, Table V (A), and no. 6, Table V (B).

A comparison of the results obtained with complexing initiators reveals a characteristic difference from those obtained with cationic initiators. The Glyc/Cap ratio is higher than 1.0 in all experiments with reaction temperatures <150 °C (Table III, and Nos. 1, 2, and 4–7, Table IV). Again, the Glyc/Cap ratios tend to 1.0 with increasing conversion; yet at low conversions high Glyc/Cap ratios or even pure poly(glycolide) were found (nos. 1, 3, and 4, Table IV). In this connection it was noteworthy that $ZnCl_2$ and $Al(O\text{-}i\text{-}Pr)_3$ give similar Glyc/Cap ratios and similar block lengths at similar yields (nos. 2 and 5, Table III). This result is one argument why we have classified zinc chloride as a complexing catalyst and not as a cationic initiator. This classification (discussed below in more detail) means that the reactive chain end is a zinc chloride containing complex and not a cation. Also, dibutyltin dimethylate favors the incorporation of glycolide at low comparisons (nos. 9–11, Table III); yet the difference of reactivity of both monomers is less pronounced than in the case of zinc chloride or aluminum isoproylate. Thus, the following three types of copolyesters are available from copolymerization with complexing initiators: (D) copolyesters with a blocky sequence and a high glycolyl/hydroxycaproyl ratio, (E) copolyesters with a blocky sequence and an equimolar composition, (F) copolyesters with a random sequence and an equimolar composition.

Finally, it is noteworthy that all four copolymerizations conducted with anionic catalysts (nos. 8–11, Table IV) agree in that exclusively poly(glycolide) was formed.

Transesterification and Reaction Mechanisms. When the sequences obtained by copolymerizations of lactones are discussed in terms of monomer reactivity and polymerization mechanisms, the role of transesterification must first be elucidated. In order to check which of the initiators used in this work catalyze intermolecular transesterification, the following experimental set was used. Poly(ϵ-caprolactone) of $\overline{DP} > 100$ was dissolved in nitrobenzene and glycolide was polymerized in this solution. The polymeric material which precipitated from the reaction mixture was subjected to ^1H and ^{13}C NMR spectroscopic analyses of molar composition and sequence (Table V). Intermolecular transesterification must result in the formation of copolyesters, i.e., in the formation of Cap–Glyc and Glyc–Cap bonds. Since the concentration of poly(ϵ-caprolactone) was constant in all experiments, whereas that of poly(glycolide) depends on the conversion, the molar ratio of Cap–Glyc and Cap–Cap bonds determined from the ^{13}C NMR signal intensities (a'/a in Figures 2 and 3) was chosen as a measure of transesterification.

The results listed in Table V clearly indicate that transesterification was only detectable for $FeCl_3$, BF_3, and FSO_3H. Its extent increased, as expected, with reaction time and temperature. It is also noteworthy that in four experiments (nos. 1, 2, 5, and 6, Table V) a Glyc/Cap ratio > 1 was obtained, which indicates a partial depolymerization of polycaprolactone. This catalytic degradation is a second indicator of the transesterification activity of the cationic catalysts. A third indication of transesterification is the presence of the triad Cap–Glyc–Cap (signal x''' in Figures 2 and 3) in several copolyesters prepared by means of cationic initiators, because ring opening of glycolide alone never can yield this sequence. As shown in Figures 2 and 3 the concentration of this triad increases with reaction time and temperature when acidic initiators were used. However, zinc chloride neither caused intermolecular transesterification (no. 11, Table V) nor fast degradation of poly(ϵ-caprolacton) nor was the triad Cap–Glyc–Cap detectable in the copolyesters nos. 1 and 2 of Table III. Because zinc chloride also favored the incorporation of glycolide in analogy with the aluminum and tin alcoholates (Table III) we classified zinc chloride as a complexing catalyst and not as a cationic (or acidic) initiator. This classification stands in contrast to the general classification as a Lewis acid. However, our results suggest that in the case of lactone polymerization all catalysts, with exception of protic acids and true anionic initiators, need closer inspection of their catalytic activities and reaction mechanisms before a reliable classification may be made. Equations 5 and 6 outline how zinc chloride could initiate



an "insertion mechanism" instead of a true cationic chain growth (eq 7). At the current state of affairs these mechanisms are merely hypothetical schemes to illustrate the problem, because a detailed investigation of polymerization mechanism is still lacking. However, in a later part of this series we will present a more comprehensive study on the mechanism of the cationic polymerization of lactones.

Another interesting result of our transesterification experiments is the lack of any intermolecular transesterification when aluminum isopropylate or dibutyltin dimethylate are used despite reaction temperatures up to 150 °C (nos. 13–16, Table V). This finding agrees with the observation that both catalysts do not cause fast degradation of poly(ϵ-caprolactone). However, the lack of intermolecular transesterification contrasts at first glance sharply with the presence of high concentrations of Cap–Glyc–Cap triads in all copolyesters prepared with these alcoholates (Figure 1). Hence, we must conclude that

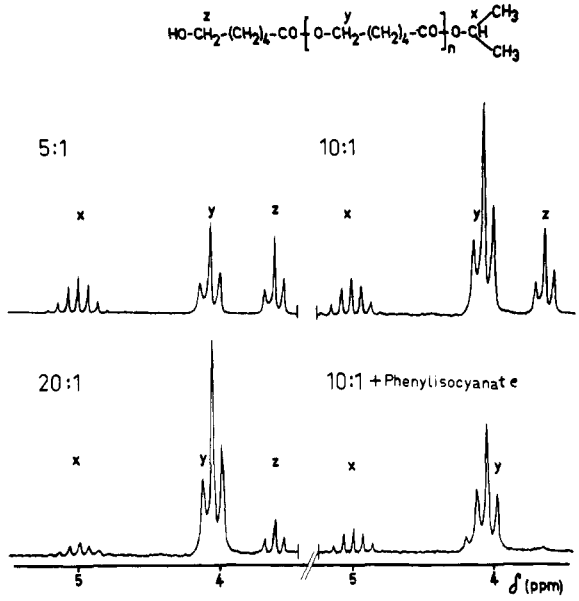
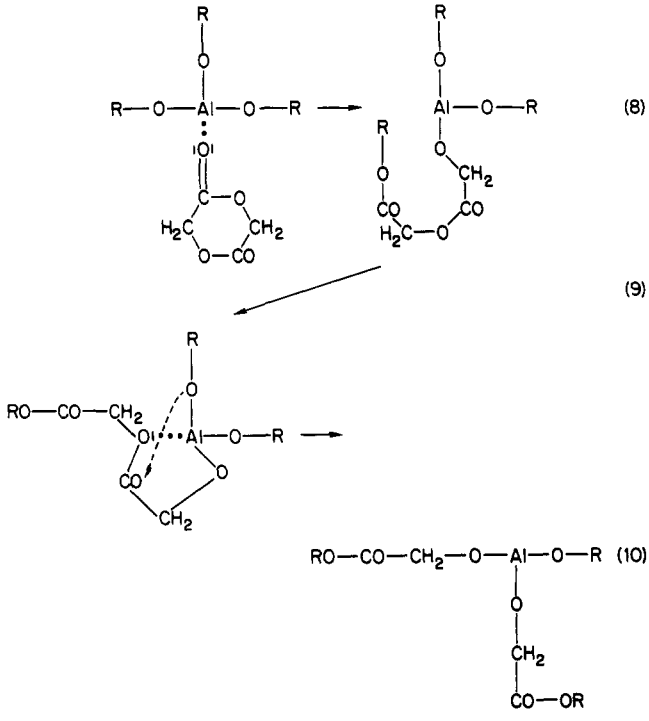


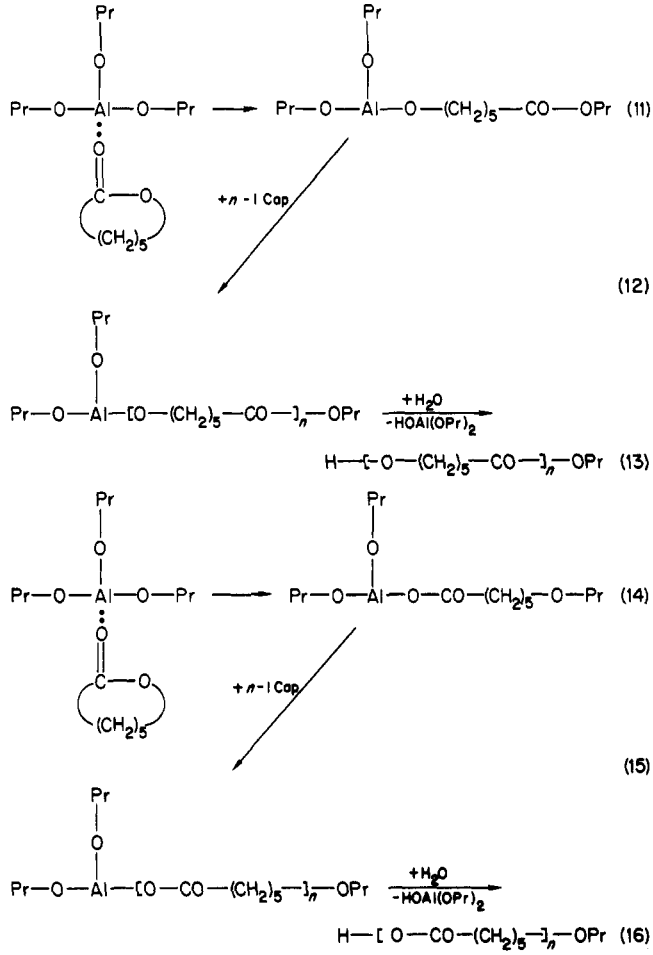
Figure 4. 90-MHz ^1H NMR spectra of poly(ϵ-caprolactones) prepared with various mole ratios of aluminum isopropylate (the spectra were measured in $CDCl_3$, and the chemical shifts referenced to internal Me_4Si).

aluminum and tin alcoholates cause frequent intramolecular transesterifications. A hypothetical mechanism which explains the intramolecular double cleavage of glycolide is outlined in eq 8–10. When the initial alcoholate group



has been replaced by a growing chain with an ϵ-hydroxycaproyl unit attached to aluminum, intramolecular cleavage of the Glyc–Glyc bond may lead to the triad Cap–Glyc–Cap.

A prerequisite of the validity of this intramolecular transesterification mechanism is, of course, a chain growth mechanism which involves the initial formation of an alkyl ester group along with the cleavage of the acyl–oxygen bond (eq 11–13). The complementary mechanism, i.e., the cleavage of the alkyl–oxygen bond and the formation of an ether end group is outlined in eq 14–16. It is obvious that the mechanistic course of these polymerizations can be determined by suitable end-group analyses. If the



mechanism of eq 8 is correct, the resulting polyester must possess one alkyl ester end group and after hydrolysis of the metal–oxygen bond one CH_2–OH end group. Assuming that Al–O bonds are easier to hydrolyze than Sn–O bonds we have studied the homopolymerization of ϵ-caprolactone by means of aluminum isopropylate. Monomer/initiator ratios of 5:1, 10:1, 20:1, and 50:1 were used and the resulting polymers were precipitated from acidic ice water so that nearly quantitative conversions and nearly quantitative precipitations were obtained, along with a quantitative hydrolysis of the initiator fragment. The resulting poly(ϵ-caprolactones) were characterized by means of ^1H and ^3C NMR spectra. The spectroscopic comparison of the poly(ϵ-caprolactones) with isopropyl butyrate and diisopropyl ether revealed that all polyester samples exclusively contained isopropyl ester end groups (Figure 4). The methine proton of the isopropyl ester absorbs ca. 0.4 ppm downfield of that of an isopropyl ether, whereas the methine carbon of the ester group absorbs ca. 6 ppm upfield of a methine ether carbon.

The ^1H NMR spectra of the four poly(ϵ-caprolactones) also displayed the triplet of an O–CH_2 group ca. 0.4 ppm upfield of the triplet assigned to the polyester O–CH_2 group. The intensity of the triplet was in all cases about twice that of the isopropyl end-group's methine proton, and thus, this triplet was assigned to the $HOCH_2$ end group (Figure 4). Further evidence for this assignment was obtained by addition of phenyl isocyanate, because the formation of an urethane group causes a downfield shift of the O–CH_2 group, so that their triplet virtually disappears due to overlapping with the more intensive triplet of the esterified (backbone) O–CH_2 groups (Figure 4). Hence, these ^1H NMR spectroscopic end-group analyses unambiguously confirm the polymerization mechanism of

eq 11 and 12. Moreover, quantification of the end groups yields still further support of the intramolecular transesterification (eq 8–10). This transesterification mechanism requires the participation of at least two alcoholate bonds, and this means that the resulting average degree of polymerization ($\overline{DP}$) must be around $^1/_3$ or $^1/_5$ of the monomer/initiator ratio. Indeed, the ^{1}H NMR end-group analyses of the isolated poly(ϵ-caprolactones) yield $\overline{DP}$s close to $(1/3)(M/I)$. In this connection it is noteworthy that the homopolymerization of ϵ-caprolactone by means of aluminum isopropylate was studied by Teyssié et al.[18,19] Our findings agree with their results and their polymerization mechanism in that Teyssié et al. also formulated an insertion mechanism with cleavage of the acyl–oxygen bond and formation of an isopropyl ester end group. However, two slight differences are to be mentioned. Teyssié et al. postulated a complexation of the lactone at the "ether oxygen", whereas we prefer to formulate the first complexation with the carbonyl oxygen (eq 8, 11, and 14), because the carbonyl oxygen is the most basic[20,21] and most nucleophilic site of an ester group. Furthermore, Teyssié et al. demonstrate that only one alcoholate group of the initiator is active when the polymerizations are conducted at 0 °C in nonpolar solvents. They also demonstrate that association of aluminum isopropylate is responsible for the limited activity of the isopropylate groups. Since we used a polar solvent and much higher reaction temperatures, dissociation of the initiator molecules and activation of all three isopropylate is obvious.

Crystallinity and Chemical Heterogeneity. The ^{13}C NMR sequence analyses indicate that copolyesters of largely differing Gly–Cap sequences can be prepared by variation of the initiator and the reaction conditions. These different sequences are expected to influence the properties of the copolyesters. The analogous poly(ϵ-caprolactone) copolyesters with a nearly random sequence of Glyc and Cap units are soluble in several nonacidic solvents, such as chloroform. With increasing block length of the Glyc units the solubility decreases and increasing concentrations of trifluoroacetic acid (TFA) are needed to bring about complete solubility. At block lengths above 15 the copolyesters are insoluble even in pure TFA, like pure poly(glycolide). These broadly varying solubilities suggest that even relatively short glycolide blocks form crystalline domains.

In order to check the crystallinity of various types of Glyc–Cap sequences, differential scanning calorimetry (DSC) measurements were conducted. The DSC traces of the corresponding homopolymers (Figure 5a,c) indicate a high degree of crystallinity because glass transitions were not detected. The DSC curve of copolyester no. 14, Table I (Figure 5c) displays a distinct endotherm at 51 °C, slightly below the "melting point" of pure poly(ϵ-caprolactone), whereas an endotherm of crystalline Glyc blocks is not detectable, in good agreement with the average block lengths ($\bar{L}_C$ = 11.7; $\bar{L}_G$ = 2.0). The inverse pattern is observable for copolyester no. 4, Table III ($\bar{L}_C$ = 2.5; $\bar{L}_G$ = 14.2). In this case a weak endotherm is detectable at 47 °C, despite the low average block length of Cap units. The copolyester no. 9 (Table I), which possesses nearly equal block lengths of both comonomers [$\bar{L}_C$ = 9.5; $\bar{L}_G$ = 8.7) displays two melting endotherms, and again a glass transition seems to be lacking (Figure 5e). Curve e (like curves b and c) displays endotherms with two peaks, which coalesce into one peak after cooling and reheating (Figure 5f). Obviously, the two peaks result from crystallites of different size. The finding that the melting endotherms of the copolyesters show up several degrees below those

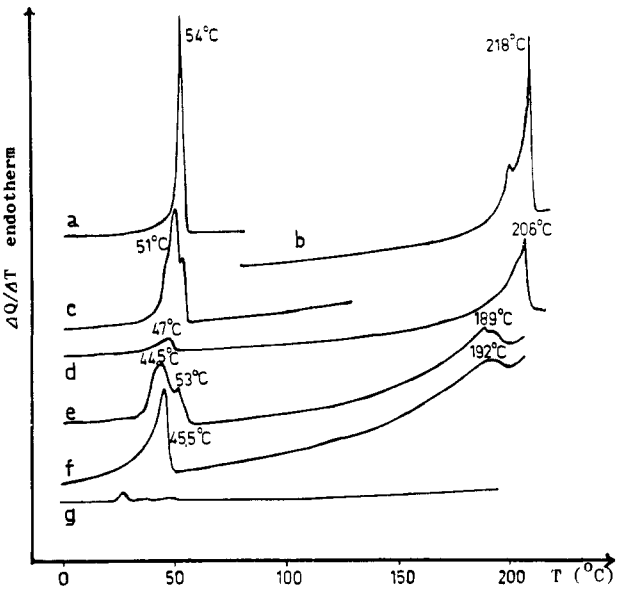


Figure 5. Differential scanning calorimetry measurements obtained at a heating rate of 20 °C/min: (a) poly(ϵ-caprolactone); (b) poly(glycolide); (c) copolyester no. 14, Table I; (d) copolyester no. 4, Table III; (e) copolyester no. 9, Table I; (f) copolyester no. 9, Table I second heating; (g) copolyester no. 2, Table I.

of the two homopolyesters may have two reasons, smaller crystallites or lower perfection of crystallites due to the incorporation of comonomers. The latter factor seems to prevail, because annealing or reheating does not shift the copolyester endotherms up to the position of the homopolymer endotherms. Finally, it is satisfying to find that copolyester no. 2, Table I, which apparently possesses a truly random sequence did not exhibit any distinct endotherm.

The X-ray powder patterns of the same samples were found to be in good agreement with the DSC measurements. Copolyesters with distinct melting endotherms either show the reflexes of crystalline polyglycolide (2ϑ = 29.2° and 22.5°) or of crystalline poly(ϵ-caprolactone) (2ϑ = 24.2° and 21.6°) or the reflexes of both crystal lattices (sample no. 9, Table I). However, the powder pattern of the random copolyester no. 2, Table I, only displays the diffuse halo of an amorphous material.

The observation that an average block length of 8–9 suffices for the formation of crystalline domains may be understood on the basis of a monomodal block length distribution because the nucleation of the crystal growth may result from the few long blocks with more than 20 monomer units. However, the melting endotherm at 47 °C of sample no. 4, Table III, is difficult to understand because an average block length of Cap units around 2.5 along with a low Cap/Glyc ratio does not justify the crystallization of Cap blocks unless considerable chemical heterogeneity of first or second order is present. Whereas we were not able to elucidate the chemical heterogeneity of second order, fractionation of the copolyesters should reveal the existence of chemical heterogeneity of first order. Dimethylformamide (DMF) was found to be a suitable solvent for this purpose. The results listed in Table VI suggest again that the initiators can be subdivided into two classes, the cationic and the complexing initiators. The copolyesters prepared by means of $FeCl_3$, BF_3, and FSO_3H were completely soluble in DMF despite different average block length. This finding indicates the absence of strong chemical heterogeneity of first order, and this result fits in well with the detection of intermolecular transesterification.

Zinc chloride, aluminum isopropylate, and, interestingly, aluminum chloride yielded copolyesters which gave a DMF-soluble and a DMF-insoluble fraction. The molar Glyc/Cap ratio of the soluble fraction was lower than that of the insoluble fraction and higher than the Glyc/Cap ratio of the original sample (Table VI). This fractionation clearly proves that the samples nos. 7–12, Table VI, are heterogeneous with respect to composition and sequence of the polyester chains. The extent of this heterogeneity is best demonstrated by comparison of the Glyc/Cap ratios of the soluble and insoluble fractions which in the case of samples nos. 9–12 differ by a factor 10!

Since all three initiators favor the incorporation of glycolide (Table VI) in contrast to the cationic catalysts, the course of the copolymerizations may approximately be described by defining the following three stages. At first a homopolymerization of glycolide sets in, which is gradually followed by a true copolymerization, which in the case of aluminum isopropylate favors the formation of Cap–Glyc–Cap triads (signal x''' in Figure 1). The consumption of glycolide leads to the third stage, i.e., the homopolymerization of ϵ-caprolactone. Due to the absence of intermolecular transesterification the blocky sequences are not subjected to equilibration. Hence, samples with a high Glyc/Cap ratio and relatively short average block lengths of Cap units may well contain long Cap blocks which are responsible for the melting endotherms in the range of 45–53 °C (Figure 5d).

Finally, it is noteworthy that aluminum chloride behaves in the experiments of Table VI like zinc chloride and aluminum isopropylate and not like the cationic initiators. Thus, the results of Table VI confirm those of Table I. Apparently aluminum chloride reacts with lactones in such a way that at least one Al–Cl bond is replaced by an Al–O bond, so that finally an insertion mechanism takes place in analogy with the mechanism formulated for zinc chloride (eq 5 and 6). Since clear-cut experimental evidence for such a mechanism is still lacking, we only want to point to the problem that not all so-called Lewis acids automatically initiate cationic polymerizations of lactones.

Conclusions

The present NMR spectroscopic analyses of glycolide /ϵ-caprolactone copolymers show that, depending on the temperature and on the nature of the initiator, copolyesters with a broad variety of molar composition and sequence can be synthesized. Acidic catalysts initiate cationic copolymerization yielding copolyesters richer in caprolactone. Complexing catalysts initiate an insertion mechanism which favors the incorporation of glycolide, whereas anionic catalysts exclusively initiate the homopolymerization of glycolide. The combination of end-group and sequence analyses provides new insight into the polymerization mechanisms and suggests that the conventional classification[22] of initiators must be reconsidered with respect to the polymerization of lactones. In contrast to acidic catalysts, complexing initiators do not cause intermolecular transesterification and yield copolyesters with a high degree of chemical heterogeneity of first order. With knowledge of molar composition, sequence, and chemical heterogeneity, other properties such as solubility and crystallinity (as revealed by DSC and X-ray measurements) are more easily understandable.

Acknowledgment. We thank the Deutsche Forschungsgemeinschaft for financial support.

Registry No. $FeCl_3$, 7705-08-0; $AlCl_3$, 7446-70-0; $PF_3{\cdot}Et_2O$, 109-63-7; FSO_3H, 7789-21-1; $ZnCl_2$, 7646-85-7; $Al(O\text{-}i\text{-}Pr)_3$, 1100-88-5; $(n\text{-}Bu)_2Sn(OMe)_2$, 1067-55-6; Phe_3P^+-Bzl·Cl^-, 1100-88-5; Et_4N^+-benzoate, 16909-22-1; (glycolide)·(ϵ-caprolactone) (copolymer), 41706-81-4; poly(ϵ-caprolactone) (homopolymer), 24980-41-4; poly(glycolide) (homopolymer), 26202-08-4; poly(ϵ-caprolactone) (SRU), 25248-42-4; ϵ-caprolactone, 502-44-3; glycolide, 502-97-6; poly(glycolide) (SRU), 26009-03-0.

References and Notes

(1) Wise, D. L.; Fellmann, T. D.; Sanderson, J. E.; Wentworth, R. L. In "Drug Carriers in Biology and Medicine", 1st ed.; Gregoriadis, G., Ed., Academic Press: New York, 1979; pp 237–270.
(2) Ethicon Inc. Ger. Offen. 2 162 900, Jan. 29, 1972; *Chem. Abstr.* **1972**, *76*, p73051*w*.
(3) Schmitt, E. E.; Polistina, R. A. U.S. Patent 3 297 033, Jan 10, 1967; U.S. Patent 3 463 158, Aug 26, 1969 (American Cyanamid Co.); *Chem. Abstr.* **1967**, *66*, p38656*u*; and *Chem. Abstr.* **1969**, *71*, p92382*t*.
(4) Pitt, C. G.; Schindler, A. E. U.S. Patent 4 148 871, Apr 10, 1979; *Chem. Abstr.* **1979**, *91*, p9512*e*.
(5) Pitt, C. G.; Gratzl, M. M.; Jeffcoat, A. R.; Zweidinger, R. A.; Schindler, A. E. *J. Pharm. Sci.* **1979**, *68*, 1534.
(6) Pitt, C. G.; Jeffcoat, A. R.; Zweidinger, R. A.; Schindler, A. E. *J. Biomed. Mater. Res.* **1979**, *13*, 497.
(7) Pitt, C. G.; Gratzl, M. M.; Kimmel, G. L.; Surless, J.; Schindler, A. E. *Biomater. (Guildford, Engl.)* **1981**, *2*, 215.
(8) Sporzynski, A.; Kocay, W.; Briscoe, H. V. A. *Recl. Trav. Chim. Pays-Bas* **1949**, *68*, 613.
(9) Kricheldorf, H. R.; Leppert, E.; Schilling, G. *Makromol. Chem.* **1974**, *175*, 1705.
(10) Kricheldorf, H. R.; Rieth, K. *J. Polym. Sci., Polym. Lett. Ed.* **1978**, *16*, 379.
(11) Kricheldorf, H. R.; Hull, W. E. *J. Polym. Sci., Polym. Chem. Ed.* **1978**, *16*, 2253.
(12) Kricheldorf, H. R.; Hull, W. E. *J. Macromol. Sci., Chem.* **1977**, *A11*, 2281.
(13) Kricheldorf, H. R.; Coutin, B.; Sekigucchi, H. *J. Polym. Sci., Polym. Chem. Ed.* **1982**, *20*, 2353.
(14) Kricheldorf, H. R.; Joshi, S. V.; Hull, W. E. *J. Polym. Sci., Polym. Chem. Ed.* **1982**, *20*, 2791.
(15) Kricheldorf, H. R. *Makromol. Chem.* **1978**, *179*, 2133.
(16) Newmark, R. A. *J. Polym. Sci., Polym. Chem. Ed.* **1980**, *18*, 559.
(17) Kricheldorf, H. R.; Dröscher, M.; Hull, W. E. *Polym. Bull. (Berlin)* **1981**, *4*, 547.
(18) Costa, G.; Locatelli, P.; Zambelli, A. *Macromolecules* **1973**, *6*, 651.
(19) Ouhadi, T.; Stevene, C.; Teyssié, P. *Makromol. Chem. Suppl.* **1975**, *1*, 191.
(20) Birchall, T.; Gillespie, J. *Can. J. Chem.* **1963**, *41*, 2642.
(21) Birchall, T.; Gillespie, J. *Can. J. Chem.* **1965**, *43*, 1045.
(22) Lundberg, R. D.; Cox, E. F. In "Ring Opening Polymerization"; 1st ed.; Frisch, K. C., Regen, S. L., Eds.; Marcel Dekker: New York and London, 1969; pp 267–268.