Macromolecules **1989**, *22*, 3275–3280 **3275**

$$P_{01} = \frac{1}{\left[2\dfrac{[000]}{[001] + [100]} + 1\right]} \qquad \text{(A18)}$$

A similar expression for P_{10} can also be obtained. Thus, from observed triad abundances, values for P_{01} and P_{10} can be calculated. Conformity to the first-order Markovian model can then be determined after a comparison of observed triad distribution with that calculated from eq A12–A17 (e.g., see results for B1, Table III).

If a successful fit is obtained, then mole fractions of 0 to 1 are given by eq A19 and A20, respectively:

$$[0] = \frac{P_{10}}{P_{01} + P_{10}} \qquad \text{(A19)}$$

$$[1] = \frac{P_{01}}{P_{01} + P_{10}} \qquad \text{(A20)}$$

Number-average sequence lengths for 0 and 1 are given by the following expressions:

$$n_0 = 1/P_{01} \qquad \text{(A21)}$$

$$n_1 = 1/P_{10} \qquad \text{(A22)}$$

Finally the relationships between the probabilities P_{00} and P_{10} and P_{01} and P_{11} prove to be particularly useful in describing the polymer microstructure. There are three possible cases.

$$\text{Case 1:} \qquad P_{10} > P_{00}, \quad P_{01} > P_{11}$$

For this case, an opposite sequence of monomer additions is favored over a like sequence of additions; i.e., there is a tendency toward an alternating copolymer.

$$\text{Case 2:} \qquad P_{10} < P_{00}, \quad P_{01} < P_{11}$$

Here a like sequence of monomer additions is favored, indicating that there is a tendency toward formation of a "blocky" copolymer.

$$\text{Case 3:} \qquad P_{10} = P_{00}, \quad P_{01} = P_{11}$$

For this case, monomer addition probabilities do not depend upon the nature of the preceding monomer unit; i.e., they reduce to a Bernoullian system, which describes a purely random comonomer distribution. Thus, any Bernoullian system can actually be described as a special case of the first-order Markov system.

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Organotin-Mediated Synthesis of Macrocyclic Tetraesters. A Combined ^{1}H NMR Spectroscopy, Gel Permeation Chromatography, and Fast Atom Bombardment Mass Spectrometry Approach to Complete Product Analysis[1]

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ABSTRACT: A complete product analysis of the reaction of 2,2-di-*n*-butyl-1,3,2-dioxastannolane with a series of diacyl dichlorides in the organotin-mediated synthesis of macrocyclic polyesters has been performed by combined ^{1}H NMR, GPC, and FABMS techniques. The experimental results provide unambiguous evidence that the product mixtures are well-behaved equilibrium distributions of cyclic oligomers, in which the absence of anomalous abundance for any of the macrocyclic products points to the lack of selectivity features that might be ascribed to a tin-template effect, as suggested by other authors.

Introduction

The reaction of cyclic stannoxanes such as 2,2-di-*n*-butyl-1,3,2-dioxastannolane (**1**) with diacyl dichlorides (**2**) has been reported by Shanzer and co-workers[2] as a convenient, one-pot procedure for the selective synthesis of macrocyclic dimeric tetraesters (**3**, $n = 2$) of reflection symmetry (eq 1). The reaction was supposed to take advantage of the ability of tin to act as a covalent template in the dimeric structure of **1** in solution. Consistently, exclusive formation of the dimeric tetraesters **3**, $n = 2$, and other remarkable selectivity features were believed to arise from the ability of the tin template to assemble the reacting molecules in

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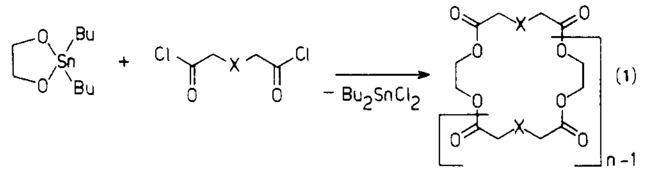

(1)

1 2 3

the final tetraester structure.[2]

In a recent investigation of the mechanism of the reaction of 1 with the dichlorides of diglycolic acid and glutaric acid (2, X = O and CH_2, respectively), one of us[3] has found, on the basis of ^1H NMR spectroscopy and thin-layer chromatography evidence, that the cyclic dimers 3, $n = 2$, were not the sole components of the reaction mixtures but only the most abundant among several ester products. The cyclic nature of the latter products was suggested but could not be directly proved. Furthermore, unambiguous evidence was obtained that the reaction mixtures were under thermodynamic control, as a result of fast transesterification processes taking place under the mild reactions conditions. This should lead to an equilibrium distribution of polymeric materials in which the occurrence of a whole family of macrocyclic oligomers is either exclusive or significant,[4,5] as predicted by the theory of Jacobson–Stockmayer (JS).[6]

The above findings and considerations not only show that the very statement that macrocyclic tetraesters are formed as sole ring products is incorrect but also cast serious doubts on Shanzer's mechanistic conclusions about the templating role of tin.

Since a careful product analysis is preliminary to any mechanistic description of a given reaction, we have carried out an extensive investigation of the products formed in reactions of 1 with diglycolyl (2, X = O), glutaryl (2, X = CH_2), adipoyl 2, X = $(CH_2)_2$, and sebacoyl [2, X = $(CH_2)_6$] dichlorides in $CHCl_3$ solution. A combination of ^1H NMR, gel permeation chromatography (GPC), and FABMS techniques was used to obtain a consistent set of data. The results of this investigation, together with a comparison with predictions from JS theory, are reported herein.

Experimental Section

Most of the materials used in this work have been described in detail elsewhere.[3] Adipoyl and sebacoyl dichlorides (Fluka) were purified by fractional distillation under vacuum.

Cyclization Procedure. The reactions were carried out by adding under nitrogen a $CDCl_3$ solution of 2 to an ice-cooled equimolar solution of 1, dissolved in the same amount of $CDCl_3$. After the addition, the solution was stirred at room temperature to ensure complete reaction, which took a few hours for the most dilute runs. ^1H NMR spectra were taken directly from the above solutions, without any further treatment. Samples of GPC and FABMS analyses were freed from Bu_2SnCl_2 by distillation under vacuum.

^{1}H NMR Spectra, GPC Analyses, and FAB Mass Spectra. ^1H NMR spectra were carried out on a Varian VXR 300 instrument. Chemical shift values (δ) are given in ppm fro Me_4Si, using $CHCl_3$ ($\delta = 7.26$) as internal secondary reference. Acquisition times of 3.8 s (0.001 ppm digital resolution), small pulse width (PW < 30°), and delays (10 s) were used for the acquisition of spectra.

A Waters 6000 A apparatus equipped with a series of four microstyragel columns (in the order 1000-, 500-, 10 000-, and 100-Å pore size) was used for GPC analyses. A Model R 401 differential refractometer from Waters was used as detector. Analyses were performed at 25 °C using tetrahydrofuran (THF) as eluant at a flow rate of 0.7 mL/min.

FAB mass spectra were performed on a double-focusing Kratos MS 50 S mass spectrometer equipped with the standard FAB source. Mass spectra were recorded by using a UV recorder. Xenon was used as bombarding gas, with an energy of 8 kV. Mass resolution was approximately 2000. A mixture of CsI/RbI (50/50 wt/wt) was used as calibrant (calibration range: m/z 28–1900). Spectra were obtained by using 3-nitrobenzyl alcohol as matrix. Positive ions emitted during FAB analyses of mixtures were recorded immediately upon introduction of the sample. B/E-FAB spectra were performed by using a linked scan unit,[7] at a scan rate of 30 s/decade, and recorded on a UV recorder.

Results and Discussion

In a typical set of experiments, the initial concentrations of the two reacting monomers (after mixing) were 0.42 mol L^{-1}. The resulting reaction mixtures were systematically subjected to ^1H NMR, FABMS, and GPC analyses. Consistent with previous experiments,[3] the ^1H NMR spectra showed that, in addition to the stoichiometric amount of Bu_2SnCl_2, only ester products were formed, which appeared as complex mixtures of different compounds, with some degree of resolution for the lower members of the series (see below). Positive ions emitted in the FABMS analyses of the reaction mixtures revealed patterns typical of homologous series of cyclic polyesters (Figure 1). The gel permeation chromatograms consisted in all cases of a broad band due to high molecular weight unresolved material, followed by a series of fairly resolved peaks whose intensity and resolution regularly increased on increasing elution volume. The GPC trace shown in Figure 2 for poly(ethylene glutarate) is typical. The lowest molecular weight oligomer detected in each case is the cyclic dimer. This was shown in the poly(ethylene diglycolate) case by direct comparison with the elution volume of a pure sample of 3, X = O, $n = 2$,[3] and in the other cases by collection of the products corresponding to the last GPC peak (highest elution volume) followed by FABMS analysis of the collected material.[8] On the basis of the above assignments, the other peaks in the GPC traces were identified as cyclic trimer, tetramer, pentamer, and so on. The good linear dependence of the GPC elution volumes as a function of log M for the four polyester systems considered (Figure 3) is fully consistent with the conclusion that the peaks in the GPC traces are due to oligomeric members of the same homologous series.[9]

Data from GPC and FABMS analyses are collected in Table I. Relative intensities of peaks in the FABMS spectra are not reported because of the occurrence of secondary fragmentation phenomena, which systematically alter the oligomer distributions.[8]

It is of interest to compare the results from the present investigation with predictions from JS theory.[4-6] In polymer systems in which there is an equilibrium between ring and chain molecules the fundamental quantity is the molar cyclization equilibrium constant K_n, which is defined by eq 2, where $-M_m-$ and $-M_{m-n}-$ are the m-meric and

$$K_n = [-M_{m-n}-][C_n]/[-M_m-] \tag{2}$$

$(m-n)$-meric chain molecules, and C_n is the cyclic n-mer. Equation 2 can be put in the form of eq 3, where p is the

$$K_n = [C_n]/p^n \tag{3}$$

extent of reaction of functional groups in the linear part of the polymer. For most of the systems of actual interest p is so close to unity that eq 4 is a useful approximation.

$$K_n = [C_n] \tag{4}$$

Theoretical expressions that have been derived from chains obeying Gaussian statistics show that K_n varies inversely to the 5/2 power of the polymerization degree n (eq 5), where A is a function of the chemical nature of the chain and of the solvent.

$$K_n = An^{-5/2} \tag{5}$$

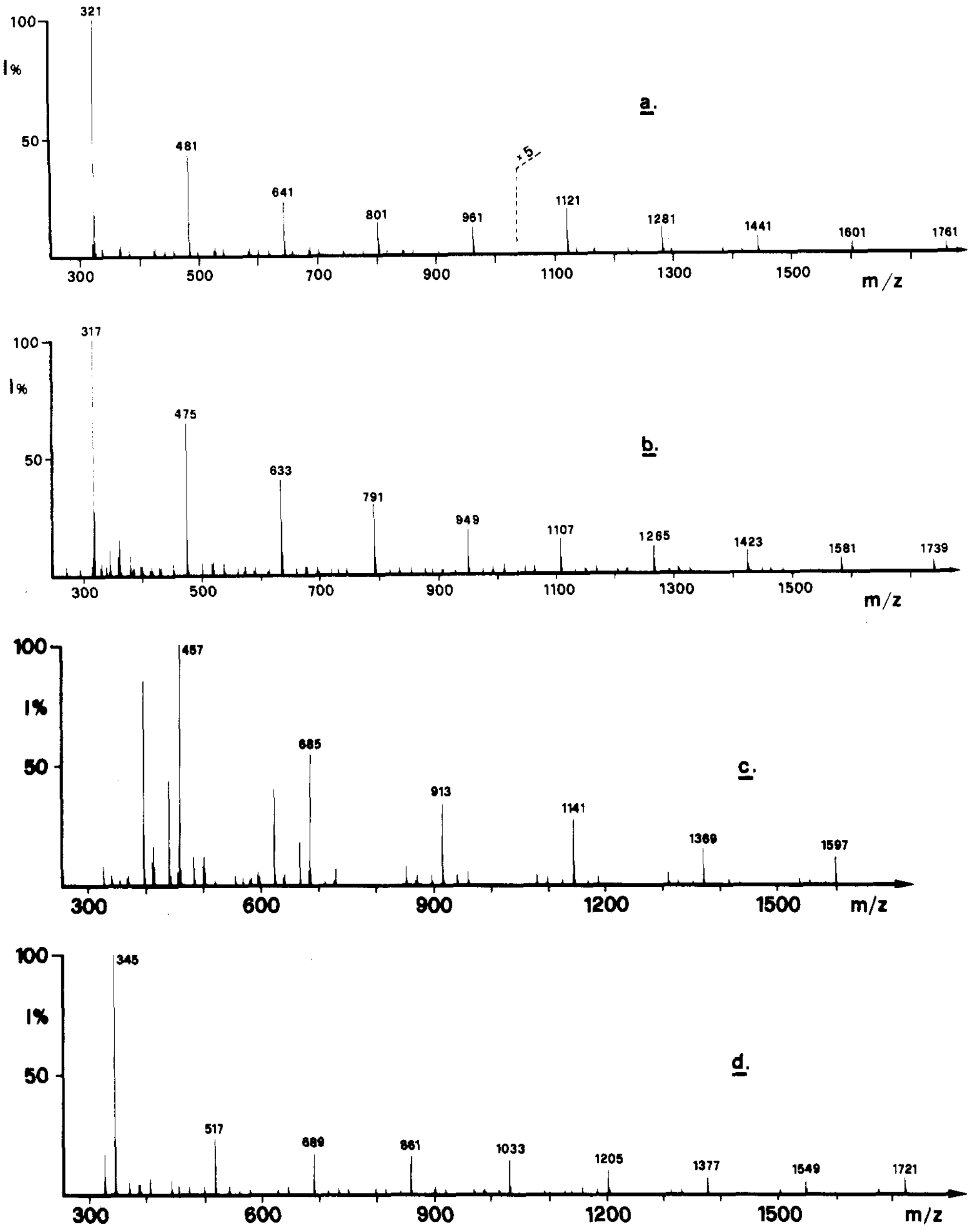

Figure 1. Positive FABMS spectra of cyclic oligomers present in (a) poly(ethylene diglycolate), (b) poly(ethylene glutarate), (c) poly(ethylene subacate), (d) poly(ethylene adipate).

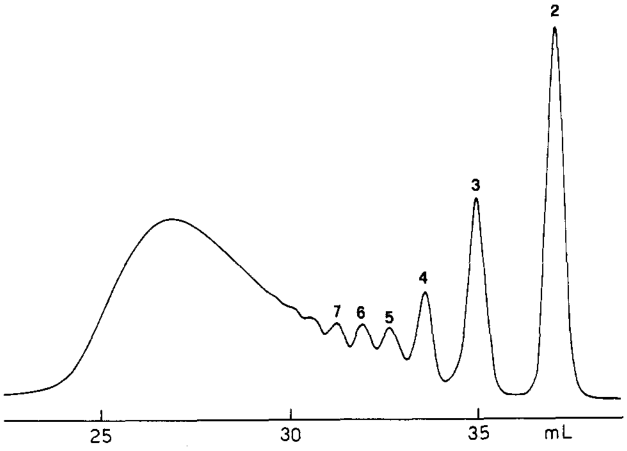

Figure 2. Gel permeation chromatogram (THF as eluant) of poly(ethylene glutarate). The numbers indicate the polymerization degree n of the cyclic oligomers.

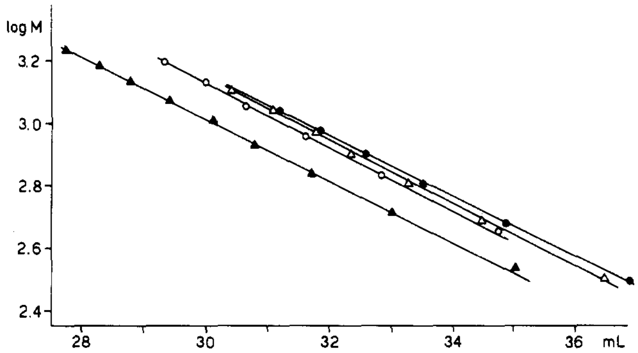

Figure 3. Dependence of the elution volume on molecular weight M of the cyclic oligomers: (●) poly(ethylene glutarate); (△) poly(ethylene diglycolate); (○) poly(ethylene sebacate); (▲) poly(ethylene adipate).

An interesting property clearly anticipated by JS theory and amply verified in a number of real systems[4] is that there is a critical monomer concentration below which the stable system is one composed of 100% rings of finite size. Thus, 2–5 strictly apply only to systems for which the monomer concentration is well above critical.

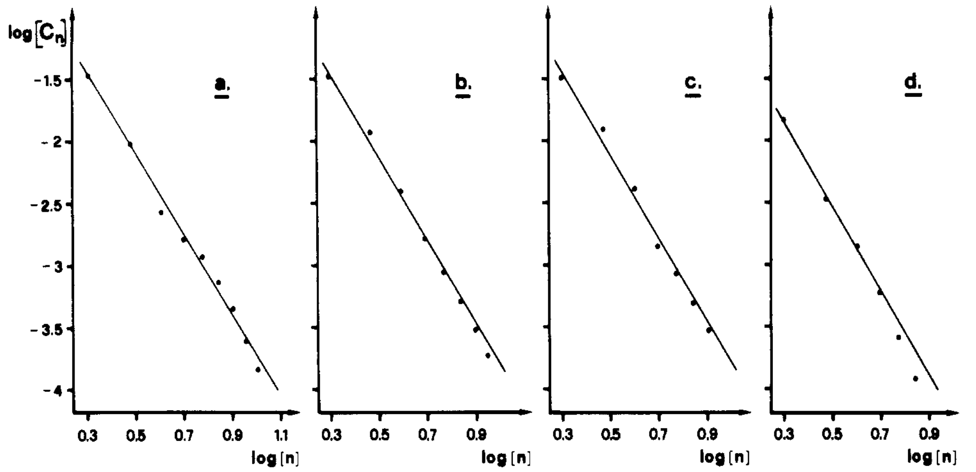

Figure 4. Logarithmic plot of molar concentration of oligomers vs polymerization degree n: (a) adipates; (b) glutarates; (c) diglycolates; (d) sebacates. Data from Table I.

Table I
GPC and FABMS Data of Cyclic Oligomers Obtained in the Reactions of 1 with 2, X = O, CH$_2$, (CH$_2$)$_2$, and (CH$_2$)$_6$

cyclic oligomers 3	n	GPC vol eluted,[a] mL	GPC %[b]	FABS m/z[c]
sebacates, X = (CH$_2$)$_6$	2	34.93	6.8	457
	3	32.86	2.4	685
	4	31.58	1.3	913
	5	30.67	0.70	1141
	6	30.02	0.32	1369
	7	29.33	0.16	1597
	8	23.45	88.40[d]	
adipates, X = (CH$_2$)$_2$	2	35.21	15.2	345
	3	33.01	6.6	517
	4	31.70	2.2	689
	5	30.80	1.8	861
	6	30.13	1.6	1033
	7	29.41	1.2	1205
	8	28.78	0.82	1377
	9	28.28	0.50	1549
	10	27.75	0.30	1721
	11	25.62	69.80[d]	
glutarates, X = CH$_2$	2	36.92	15.5	317
	3	34.92	8.8	475
	4	33.53	3.7	633
	5	32.61	1.9	791
	6	31.86	1.2	949
	7	31.21	0.82	1107
	8	30.52	0.55	1265
	9	30.01	0.36	1423
	10	26.95	67.20[d]	1581
	11			1739
diglycolates, X = O	2	36.48	14.5	321
	3	34.45	9.8	481
	4	33.26	4.1	641
	5	32.35	1.5	801
	6	31.78	1.2	961
	7	31.12	0.78	1121
	8	30.45	0.52	1281
	9	29.19	67.60[d]	1441
	10			1601
	11			1761

[a] THF was used as solvent. [b] Calculated with respect to the total area. [c] Molecular ion $(M + 1)^+$ in positive FAB spectrum. [d] Abundances corresponding to unresolved oligomers having $n \geq 8$, 11, 10, and 9, respectively.

Table II
Effect of Initial Monomer Concentration on the Distribution of the Lowest Oligomers in the Reaction of 1 with 2, X = O

monomer concn,[a] mol L^{-1}	%$_b$ (molar concn [C_n], mol L^{-1}) of cyclic oligomer $n = 1$	$n = 2$	$n = 3$	$n = 4$	$n \geq 5$
0.042	2	36 (0.0076)	17 (0.0024)	9 (0.001)	36
0.12	3	25 (0.015)	11 (0.0043)	8 (0.0025)	53
0.23	2	21 (0.024)	10 (0.0077)	7 (0.0040)	60
0.42	ca. 1	15 (0.032)	7 (0.010)	4 (0.0042)	73
0.85	<1	8.5 (0.036)	4 (0.011)	2 (0.0043)	85

[a] Monomer concentration = $[1]_0 = [2, X = O]_0$. [b] Calculated with respect to the total area in the COOCH_2 region of the ^{1}H NMR spectra (Figure 5).

Figure 4 shows logarithmic plots of molar concentrations [C_n] calculated from the weight fractions of cyclic oligomers determined from the GPC experiments against polymerization degree. The four plots are reasonably linear, but the slopes are in all cases close to −3.4, instead of the −2.5 predicted by eq 5. Thus, yields of cyclic oligomers apparently decrease upon increasing molecular weight more rapidly than predicted by JS theory.

As a possible source of this discrepancy, experimental uncertainties in the integration of peaks in the GPC traces should be taken into account, because resolution between the m- and (m+1)-mer becomes increasingly lower upon increasing m. This would easily lead to heavily underestimated values for the larger rings. Another possible reason might be that the monomer concentration of 0.42 mol L^{-1} used in the cyclization experiments is not sufficiently high to satisfy the JS conditions. As clearly anticipated by JS theory,[6] although only qualitatively, the result of diluting beyond critical is the decrease of the average size of ring molecules, i.e., the increase of the yield of the lowest oligomers at the expenses of the highest ones.

To test the validity of the latter hypothesis, we have carried out a systematic scrutiny of the effect of varying the initial reactant concentrations on yields of cyclic oligomers formed in the reaction of 1 with diglycolyl dichloride (2, X = O). In these experiments, the initial monomer concentration varied in the range 0.042–0.85 mol L^{-1}, the latter being the highest concentration allowed by the solubility of 1. Reaction mixtures were conveniently analyzed by ^{1}H NMR, which showed resolved signals for the dimer, trimer, and tetramer (Figure 5). Trace amounts of the monomeric diester were also detected in the more dilute runs.[10] The results are collected in Table II and graphically shown in Figure 6. The most remarkable feature is that the concentrations of the cyclic dimer, trimer, and tetramer approach constant values upon increasing concentration. This is in line with predictions from the JS theory for systems approaching the critical

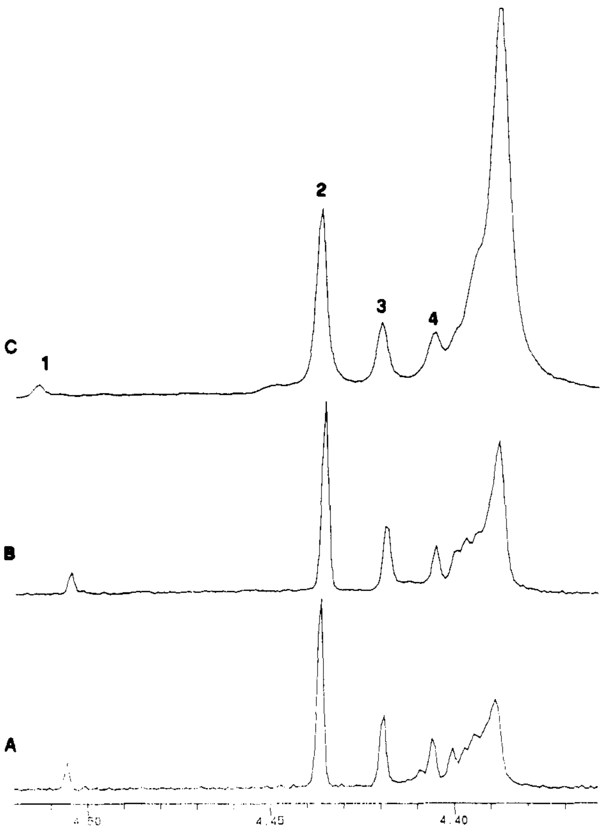

Figure 5. ^1H NMR spectra of poly(ethylene diglycolate) at varying initial monomer concentrations: (A) 0.12 mol L^{-1}; (B) 0.23 mol L^{-1}; (C) 0.42 mol L^{-1}. The numbers indicate the polymerization degree n of the cyclic oligomers.

concentration value.[6] A similar behavior has been reported by Kawakami and co-workers in a thorough study of equilibrium polymerizations of macrocyclic formals.[11]

Unfortunately, because of a lack of direct evidence of open-chain polymeric material,[10] the critical monomer concentration cannot be determined. Nevertheless, we believe that the monomer concentration in the most concentrated run (0.85 mol L^{-1}) is so close to critical that the corresponding $[C_n]$ values listed in Table II for $n = 1-4$ provide a satisfactory estimate for the pertinent K_n values.

It is of interest to compare the $[C_n]$ values from the run with initial concentration of 0.85 mol L^{-1} (Table II) with the large number of effective molarity (EM)[12] data available for various cyclization reactions over a wide range of ring sizes.[13-15] The most remarkable feature in these data is that the EM values in the neighborhood of ring size 15–25 tend to cluster in the fairly limited range of 0.1–0.01 mol L^{-1}, with a gross average value of 0.03 mol L^{-1}, showing that the ease of formation of a large ring is essentially independent of the nature of end groups and largely reflects the conformational entropy loss upon cyclization.[14,15] We now note that the $[C_n]$ values of 0.036 and 0.011 mol L^{-1} related to the formation of the dimer (18-ring) and trimer (27-ring), respectively, compare well with available EM values for rings of similar size. We also note that the molar concentration of the monomer (9-ring) of about 0.004 mol L^{-1} appears quite a reasonable value for the EM of a medium-ring where most, but not all, of the unfavorable interactions responsible for extremely low cyclization tendencies in other series have been relieved by the presence of oxygen atoms and trigonal groups in the backbone.[14,15]

Small signals that could be reasonably assigned to the monomeric rings were also present in the ^1H NMR spectra of the other reaction mixtures (initial concentrations 0.42 mol L^{-1}) in about 1, 2, and 3% yield (calculated with respect to the total area) for the glutarate, adipate, and sebacate case, respectively. These data can be translated as above into rough EM (K_1) values of 0.004 (9-ring), 0.008 (10-ring), and 0.012 mol L^{-1} (14-ring), which again turn out to be of the correct order of magnitude for the given ring sizes. It appears therefore that the essential absence of the monomeric ring products under the relatively high concentrations conditions of our experiments is a natural consequence of their low EMs.

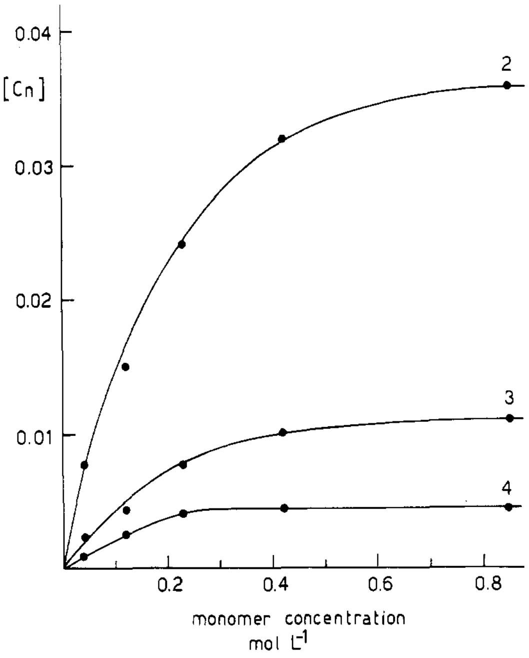

Figure 6. Equilibrium molar concentrations of cyclic dimer, trimer, and tetramer as a function of initial monomer concentration for the poly(ethylene diglycolate) system.

Concluding Remarks. The results reported in this work have unambiguously shown that the components of the reaction mixtures appearing as sets of fairly resolved peaks in the GPC traces are constituted by a series of cyclic oligomers. The experiments are elusive with respect to the linear part of the polymer, possibly present in the more concentrated runs.

Although a close adherence of the data to eq 5 could not be verified because of the possible concurrence of several factors, there seems to be little doubt that the systems investigated represent genuine examples of macrocyclization equilibria, whose behavior is in essential agreement with predictions from the JS theory.

Since the monomeric diesters cannot be formed in more than minute amounts under the conditions of our experiments because of their low EMs, the dimeric tetraester are the naturally most abundant oligomers in all of the reactions investigated. It appears therefore, although the synthetic merits of the reaction are out of question, that the lack of anomalous abundance for any of the macrocyclic products of the distribution in any of the investigated systems rules out the operation of special effects, such as a tin template effect, which would selectively enhance the formation of a particular oligomer.

Acknowledgment. Financial support by the Ministero della Pubblica Istruzione is greatly acknowledged.

Registry No. **3** (X = $(CH_2)_6$, $n = 2$, copolymer), 119771-10-7; **3** (X = $(CH_2)_6$, $n = 2$, SRU), 25034-96-2; **3** (X = $(CH_2)_2$, $n = 2$, copolymer), 119771-11-8; **3** (X = $(CH_2)_2$, $n = 2$, SRU), 24937-05-1; **3** (X = CH_2, $n = 2$, copolymer), 119771-12-9; **3** (X = CH_2, n =

2, SRU), 24938-90-7; **3** (X = O, *n* = 2, copolymer), 119771-13-0; **3** (X = O, *n* = 2, SRU), 56549-54-3.

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One-Dimensional Aromatic Crystals in Solution. 9. Synthesis, Conformation, and Chiroptical Spectroscopy of Poly[Lys(Z)$_2$-pyrAla] in Solution[1]

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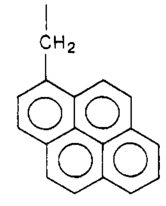
ABSTRACT: A sequential polypeptide having a repeating unit of [Lys(Z)$_2$-pyrAla] was synthesized [Lys(Z) = $^\epsilon$*N*-benzyloxycarbonyl-L-lysine, pyrAla = L-1-pyrenylalanine]. The polypeptide main chain was in a right-handed α-helical form in trimethyl phosphate solution. A one-dimensional array of pyrenyl groups along the helix was suggested from a side-chain conformational energy calculation and a theoretical circular dichroism calculation. The fluorescence spectra consisted of a monomer and a less intense excimer emission. The excimer emission was strongly left circularly polarized. The chiral configuration of the excimer indicated that the excimer is formed at an excimer-forming site located at the middle part of the helix.

A helical polypeptide chain, being rigid and regular, has been shown to be a good framework to support chromophores, keeping specific distance and orientation between the neighboring ones.[2,3] In the previous papers of this series, homopolypeptides of 1- and 2-naphthylalanines[4,5] and 1-pyrenylalanine[6,7] and also sequential polypeptides having 1-naphthylalanine as one of the constituents[8] have been reported. Circular dichroic (CD) spectra indicated that the chromophoric polypeptides are in helical conformations and the side chains are arranged regularly along the helix.



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Previously,[6] we have shown that poly(L-1-pyrenylalanine) [p(pyrAla), (I)] exhibited two types of excimer fluorescence: one emits around 460 nm and is right circularly polarized, the other emits at longer wavelengths than 500 nm and is left circularly polarized. The former excimer is predominant at high temperatures (60 °C), whereas the latter is favored at low temperature (3 °C). A likely reason for the multiple excimers is that each pyrenyl group in p(pyrAla) may interact with more than one neighboring group as shown by the dotted lines in Figure 1. In this sense, homopolypeptides of aromatic amino acids cannot support a one-dimensional chromophoric

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