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Synthesis of cyclic polyethers

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To avoid difficulty in the synthesis of cyclic diblock copolymers, cyclic poly(oxyethylene)s with large molecular weights have been prepared by Williamson etherification reaction. Polyethylene glycol (PEG) sodium alkoxides ($\bar{M}_n = 8000$ and 20 000) were reacted with a stoichiometric amount of 1,4-dibromobutane in *N*,*N*-dimethylformamide. No intermolecular condensation took place even at a high PEG alkoxide concentration of 10^{-2} M and the conversion of cyclic polymers was substantially 100%. Copyright © 1996 Elsevier Science Ltd.

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Introduction

Cyclic polymers are interesting materials because, in contrast to linear polymers, all structural units of the chain are chemically and physically equivalent. Two main synthetic methods are presently known for the preparation of cyclic polymers. The first method is based on simultaneous formation (step-growth polymerizations) in some macromolecular systems exhibiting ring-chain equilibrium[1]. Ring-chain equilibrium occurs whenever a functional site located at the chain end can react with a function connecting on the same chain. As predicted by Jacobson and Stockmayer[2], the probability of cyclic formation decreases with increasing chain length. Accordingly, cyclic macromolecules arising from backbiting are usually small in size[3]. The second method concerns polymers with carbon–carbon linkages in the backbone (chain-growth polymerizations). End-to-end cyclization is based upon intramolecular coupling between the active chain ends of an α,ω-dicarbanionic polymer, using an appropriate difunctional electrophile, in stoichiometric proportions. The reaction is carried out at very low concentration (10^{-5}–10^{-7} M) to favour intramolecular reaction (cyclization) with respect to intermolecular chain extension[4–6].

To avoid such experimental difficulties, we proposed a new approach to cyclic polymers with narrow molecular weight distribution[7]. The well-defined α,ω-dibromobutyl polystyrene (PS) was prepared by direct coupling of the polystyryl dianion with a large excess of 1,4-dibromobutane. End-to-end ring closure of the α,ω-dibromobutyl PS was performed by interfacial condensation between the aqueous phase (hexamethylene diamine) and the organic toluene phase (PS precursor). The limited field of reactions such as at the interface was effective for ring closure. The conversion of cyclic polymers was very high (more than 80%) at PS precursor concentration of 10^{-3} M.

In recent years attention has been paid to the synthesis of large cyclic oligomers, i.e. cyclo-esters[8] and cyclo-ethers (large crown ethers)[9]. Generally, crown esters are prepared in the laboratory by Williamson etherification reactions[10], either by reacting a ditosylate of polyethylene glycol (PEG) in the presence of a base, or by reacting a PEG, which already has the required number of oxyethylene units, with arenesulfonyl chlorides and heterogeneous KOH or NaOH. The latter one-pot method, first reported by Okahara *et al.*[11] is known to be suitable for the preparation of crown ethers from 15C5 to 24C8. This method was applied to cyclization of PEG with number-average molecular weight $\bar{M}_n = 1000$ (PEG1000) by Vitali and Masci[12]. They reported a yield of only 8% for the cyclization of PEG1000. More recently Yu *et al.*[13] have obtained yields of cyclics as high as 80% under more favourable conditions.

On the other hand, the phase segregation properties of cyclic block copolymers have been investigated using the theory of Leibler[14], ignoring the topological constraints specific to cyclic polymers[15]. It was predicted that, in the strongly segregated state, the wavelength of lamellar domains composed of rings is 0.63 times that of linear diblock lamellae with the same molecular weight. However, the quantitative nature of the predictions has never been examined in detail for neat copolymers. The information for the cyclizations of PEG with large molecular weight can be developed to the ring closure of poly(oxyethylene) (POE)–PS–POE BAB type triblock copolymers.

In this article, we present the cyclization of PEG ($\bar{M}_n = 8000$ and 20 000) by Williamson etherification reaction. PEG sodium alkoxides were reacted with 1,4-dibromobutane in *N*,*N*-dimethylformamide as functions of alkoxide concentration and molecular weight.

Experimental

Preparation of cyclic poly(oxyethylene). Cyclization of PEG was carried out according to Williamson etherification reaction. *N*,*N*-Dimethylformamide (DMF) was distilled over calcium hydride under vacuum. The commercial PEGs from Wako Pure Chemical Industries, Ltd. ($\bar{M}_n = 8000$ and 20 000) were converted into their alkoxides by the reaction of PEG with 1.5-fold excess of

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sodium hydride in DMF under nitrogen atmosphere. Subsequently, stoichiometric amount of 1,4–dibromobutane (DBB) was added to this solution and stirred at 80°C under nitrogen atmosphere. After reaction, the resulting mixture was poured into dimethyl ether. The polymers precipitated were collected, washed repeatedly with ether, and freeze-dried from benzene.

The extent of condensation and the ratio of cyclization to condensation were determined by gel permeation chromatography (g.p.c.; Tosoh HLC-8020 high-speed liquid chromatograph with tetrahydrofuran (THF) as eluent at 38°C, a TSK gel $\mathrm{GMH_{XL}}$ column and a flow rate of $1.0\,\mathrm{ml\,min^{-1}}$), with distribution functions improved by reshaping method[16].

Separation of cyclic polymers. The precipitation fractionation was carried out in the benzene–*n*-hexane system at 25°C in order to separate the cyclic polymer, while the turbidity of the PEG precursor was measured beforehand at a wavelength of 500 nm (Hitachi Perkin–Elmer 139 u.v.-vis. spectrometer). The intrinsic viscosities ($[\eta]$) of cyclic and linear polymers were measured by a Ubbelohde viscometer in THF at 38°C.

Results and discussion

Table 1 lists the reaction conditions of condensation of PEG alkoxide ($\bar{M}_n = 20\,000$) and DBB, varying the condensation time. Typical g.p.c. profile of CR13 is shown in *Figure 1*. It is found that the elution count of the main peak shifts to the side of low molecular weight compared with PEG precursor. Generally, the cyclic polymer has a smaller hydrodynamic volume than the linear precursor. It is therefore suggested that this product is a mixture of cyclic poly(oxyethylene) (POE) and PEG precursor. The molecular weight distribution of cyclic POE can be separated from the reshaped g.p.c. of the condensation product by subtracting the known distribution function of the PEG20000 precursor on a personal computer. G.p.c. distribution functions of CR13 after curve resolution are also shown in *Figure 1* (dotted lines). The extent of condensation and the ratio of cyclization to condensation [cyclization/(cyclization + polycondensation)] were estimated by the g.p.c. profiles as shown in *Table 1*. The error in the estimates of the extent of cyclic polymers through such computer analysis was at most several per cent. *Figure 2* shows the relationship between the extent of condensation or the ratio of cyclization to condensation and condensation time. After 18 h of condensation, the extent of condensation reaches 64%. Moreover, the ratio of cyclization to condensation was close to 100% in all of the experiments. Usually, the end-to-end ring closure of living α,ω-dicarbanions with difunctional electrophile reagents (homogeneous condensation) is achieved under a very low concentration (10^{-5}–$10^{-7}\,\mathrm{mol\,l^{-1}}$)[4–6]. It is remarkable that polycondensation (intermolecular condensation) has never taken place in CR11–CR15 (PEG alkoxide = $5.0 \times 10^{-3}\,\mathrm{mol\,l^{-1}}$).

Next, we examined the effect of PEG sodium alkoxide concentration on the condensation. This series of experiments was carried out in DMF at 80°C for 18 h. *Figure 3* shows the relationship between the extent of condensation or the ratio of cyclization to condensation and PEG alkoxide concentration. In the condensation reaction for PEG20000, the extent of condensation increased sharply beyond the PEG alkoxide concentration of $10^{-3}\,\mathrm{mol\,l^{-1}}$ due to the rapidity of Williamson reaction rate. It is also noticed that the ratio of cyclization to condensation was close to 100% even at the PEG alkoxide concentration of $10^{-2}\,\mathrm{mol\,l^{-1}}$. It is expected in general that the condensation of difunctional PEG alkoxide with DBB proceeds competitively with cyclization (intramolecular condensation) and polycondensation (intermolecular condensation).

We could estimate the theoretical values of chain cyclization predicted by Jacobson–Stockmayer type calculations[2]. According to the results of Deffieux *et al.*[17], the ratio between cyclic and polycondensates is given by

$$\frac{P_c}{P_2} = \left(\frac{3}{2\pi\langle r^2\rangle}\right)^{3/2} \frac{1}{N_A[C^*]} \qquad (1)$$

where P_c and P_2 are the probability of intramolecular condensation and the probability of intermolecular condensation, respectively. The $[C^*]$, $\langle r^2\rangle$, and N_A are the concentration of active ends ($\mathrm{mol\,ml^{-1}}$), the mean square end-to-end distance and Avogadro's number, respectively.

For poly(oxyethylene) we may consider, in a good solvent, $\langle r^2\rangle = 6.24 \times 10^{-17}\,M$ (M: the molecular mass)[18]. The theoretical percentages of cyclics expressed by $100[P_c/(P_c + P_2)]$ are plotted vs the PEG alkoxide concentration in *Figure 3* for PEG precursor of $M_n = 20\,000$. As may be seen, the extent of theoretical cyclization decreased with increasing the PEG alkoxide concentration. As predicted by the theory, for the same precursor concentration, the percentage of cyclics increases with decreasing precursor chain length. The relationship between the extent of condensation or the

Table 1 Reaction conditions and results of condensations of PEG alkoxide with 1,4-dibromobutane[a]

Code	PEG alkoxide[b] $10^3\,(\mathrm{mol\,l^{-1}})$	DBB[c] $10^3\,(\mathrm{mol\,l^{-1}})$	Time (h)	Extent of condensation (wt%)	Ratio of cyclization to condensation (%)
CR11	5.0	5.0	4	19.4	~ 100
CR12			8	42.7	~ 100
CR13			12	55.8	~ 100
CR14			18	64.0	~ 100
CR15			24	73.3	~ 100

[a] Condensations were carried out in DMF at 80°C

[b] $\bar{M}_n = 20\,000$

[c] 1,4-Dibromobutane

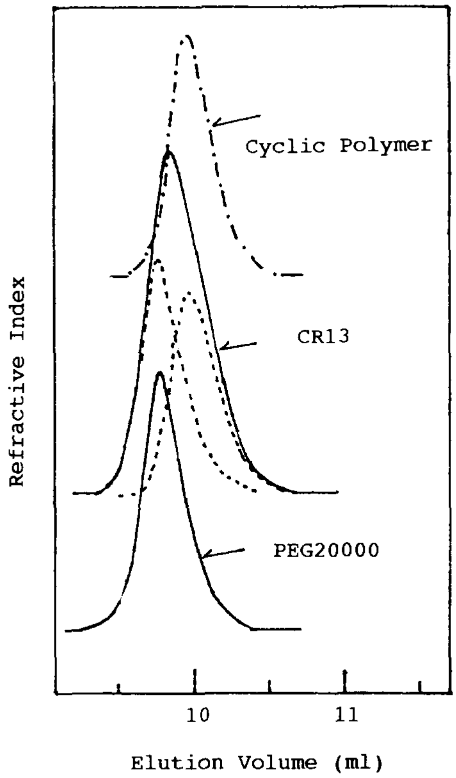

Figure 1 G.p.c. profiles of CR13, PEG20000 precursor and fractionated cyclic polymer

ratio of cyclization to condensation and PEG alkoxide ($\bar{M}_n = 8000$) concentration is also shown in *Figure 3* (dotted line for PEG8000). This series of experiments was also carried out in DMF at 80°C for 18 h. The extent of condensation increased slightly compared to that of PEG20000 series. However, the ratio of cyclization to condensation was close to 100% in the range of PEG alkoxide concentration of 10^{-3}–10^{-2} mol l^{-1}.

In order to study the solution properties of cyclic polymers, we carried out the large-scale condensation of PEG sodium alkoxide ($\bar{M}_n = 20\,000$) and DBB. G.p.c. profile of cyclic PEG after precipitation fractionation (benzene–*n*-hexane system, volume fraction of *n*-hexane = 0.43) is shown in *Figure 1*. It is found that the fraction (cyclic PEG) is separated from the PEG precursor by this fractionation and has a single molecular weight distribution.

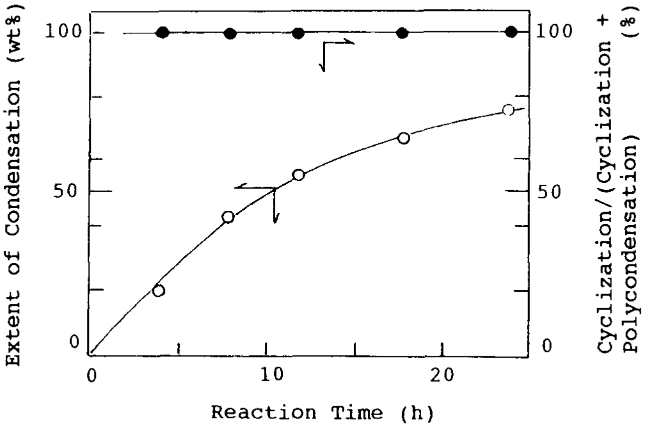

Figure 2 Relationship between extent of condensation or ratio of cyclization to condensation and condensation time

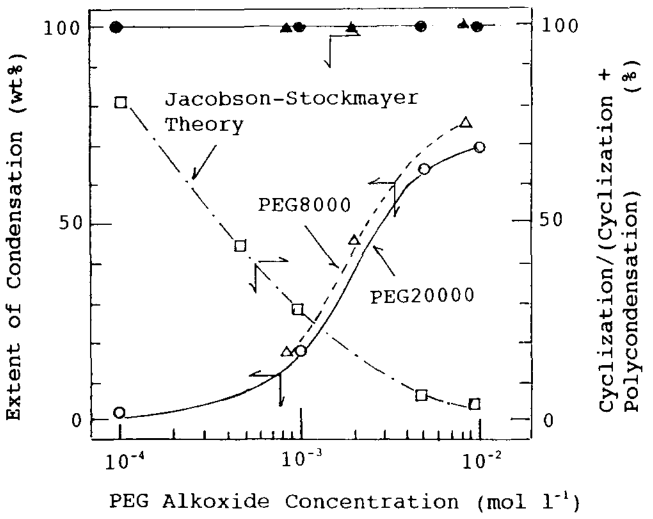

Figure 3 Relationship between extent of condensation or ratio of cyclization to condensation and PEG alkoxide concentration

We studied the viscometric properties of cyclic polymers. In order to study the ring dimensions, the shrinkage due to ring formation can be evaluated by means of the following dimensionless parameter

$$g = [\eta]/[\eta]_L \qquad (2)$$

where the subscript *L* refers to the property of the linear polymer with identical molecular weight. The intrinsic viscosity of a single-cyclic polymer has been calculated by the method of Zimm[19,20]. The value of *g* is 0.645 (non free-draining case) in the theta condition of the solvent. In the viscometric measurements, the intrinsic viscosities of cyclic PEG ($[\eta]$) and its precursor ($[\eta]_L$) were 17.7 and 27.8 ml g^{-1} in THF at 38°C, respectively. Then, the value of *g* was estimated to be 0.637. This value is well in agreement with the theoretical one in the theta solvent. Thus, the cyclic polymer has a smaller hydrodynamic dimension than the linear precursor.

Precise answer to the cause (the polycondensation has never occurred even at high concentration of PEG alkoxides) could not be obtained. It is interesting that Williamson etherification of PEG with high molecular weight proceeds predominantly with the intramolecular condensation (cyclization). We are investigating the synthesis of cyclic PS/POE block copolymers using similar method. The results obtained for their phase separation behaviours will be reported in the near future.

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