

Mechanistic Aspects of Selective Formation of 10-, 20-, and 25-Membered Macrocyclic Oligoesters in the Cationic Polymerization of 6,8-Dioxabicyclo[3.2.1]octan-7-one

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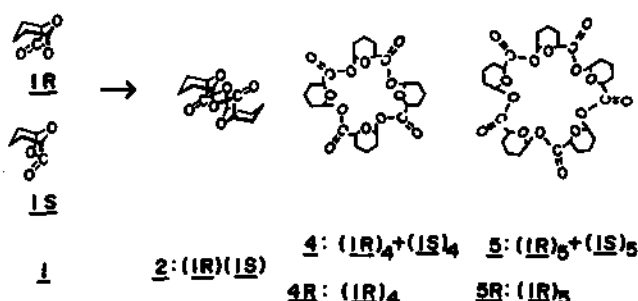
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ABSTRACT: Mechanisms of the selective formation of 10-, 20-, and 25-membered macrocyclic oligoesters (cyclic dimer, tetramer, and pentamer, respectively) from 6,8-dioxabicyclo[3.2.1]octan-7-one (1) are discussed on the basis of product distributions in the oligomerization of racemic monomer 1, optically active (+)-(1*R*,5*R*)-6,8-dioxabicyclo[3.2.1]octan-7-one (1*R*), and enantiomerically unbalanced monomer mixtures. Optically active cyclic tetramer (4*R*) and cyclic pentamer (5*R*) of 1*R* are predominantly formed by a tail-biting reaction of a growing oligomer chain, while racemic cyclic tetramer (4) and cyclic pentamer (5) are mainly produced by a back-biting reaction of an initially formed polymer of 1. Cyclic dimer (2) is formed primarily by intramolecular reaction of unsymmetrical oligomers which are formed from 4 and 5 by the reaction with monomer. All these macrocyclic oligomers are formed via an S_N2 -type mechanism involving the exclusive alkyl-oxygen fission of 1. The selective formation of 2, 4, 5, 4*R*, and 5*R* is remarkably dependent upon the reaction conditions, especially temperature, time, solvent, and optical purity of the monomer. Solubility and molecular symmetry of cyclic oligomers, interactions between a cyclic oligomer and its opposite enantiomer or a solvent molecule, and conformation of a growing chain are important factors controlling the selective formation of the cyclic oligomers of specific ring sizes.

It is not an unusual but rather common phenomenon that cyclic oligomers of various ring sizes are formed in the

cationic ring-opening polymerization of a variety of cyclic monomers.¹ These cyclic oligomers are often in equilib-

rium with their linear polymers, and the cyclic populations of some polymeric equilibrates were satisfactorily described by the Jacobson–Stockmayer equation derived on the basis of statistical treatment²⁻⁵ or by the modified expressions proposed by Flory et al.⁶⁻⁹ On the other hand, a kinetic treatment has been recently proposed by Penczek and co-workers¹⁰ to interpret time and conversion dependence of the formation of cyclic oligomers. In some cases, however, cyclic oligomers of specific ring sizes are predominantly or selectively formed, for example, cyclic tetramer from 1-benzyl-2-ethylaziridine,¹¹ cyclic tetramer from (*R*)-*tert*-butylethylene oxide,¹² and cyclic trimer and tetramer from oxetanes.¹³ Furthermore, attempts have been made to synthesize crown ethers by the ring-opening polymerization of ethylene oxide, using various metal salts as templates.¹⁴⁻¹⁶ These macrocyclic oligomers, containing heteroatoms arranged regularly in the ring structure, are expected to act as complexing agents or synthetic ionophores. Therefore, selective formation of cyclic oligomers of specific ring sizes by the ring-opening polymerization of cyclic monomers is not only interesting from the standpoint of reaction mechanism but also valuable from the standpoint of synthetic chemistry.



Recently, we found that in the cationic polymerization of racemic 6,8-dioxabicyclo[3.2.1]octan-7-one (**1**), 10-, 20-, and 25-membered cyclic oligoesters (cyclic dimer **2**, tetramer **4**, and pentamer **5**) were highly selectively formed in acetonitrile, chloroform, and 1-nitropropane, respectively, by proper selection of the reaction conditions.¹⁷⁻¹⁹ In a similar manner, optically active cyclic tetramer (**4R**) and pentamer (**5R**) of (+)-(1*R*,5*R*)-6,8-dioxabicyclo[3.2.1]octan-7-one (**1R**) were preferentially formed in acetonitrile and 1-nitropropane, respectively.²⁰⁻²² (Hereafter, **1R** denotes the enantiomer having the *R* configuration of the asymmetric carbon bearing a carbonyl group and, therefore, **1S** denotes the enantiomer having the *S* configuration of the corresponding carbon.) The macrocyclic oligoesters consist of alternating tetrahydropyran and ester moieties, and they bear structural resemblance to the naturally occurring antibiotic nonactin (a 32-membered tetrolide), which includes penetration of potassium ion, but not sodium ion, into mitochondria.²³ The present paper is chiefly concerned with mechanisms for the selective formation of these macrocyclic oligoesters from racemic monomer **1** and optically active monomer **1R**.

Experimental Section

Both the racemic monomer **1** and optically active monomer **1R** were synthesized from sodium 3,4-dihydro-2*H*-pyran-2-carboxylate.^{18,20} The polymerization procedure was described in a previous paper.¹⁸ The composition of the reaction products was determined from the relative peak areas corrected for the differences in the refractive indices of the different compounds by a JASCO TRIOTAR gel permeation chromatograph (column, JASCO JSP101, 50 cm; eluent, chloroform). IR spectra were

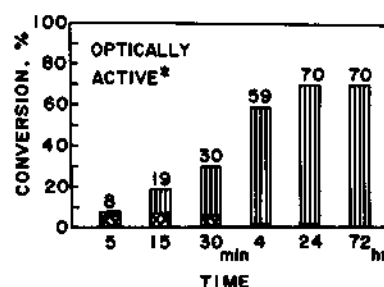


Figure 1. Time-conversion diagram for the oligomerization of (+)-(1*R*,5*R*)-6,8-dioxabicyclo[3.2.1]octan-7-one (**1R**) in 1-nitropropane. Monomer, 1 g; 1-nitropropane, 2 mL; $\text{BF}_3\cdot\text{OEt}_2$, 1 mol % to monomer; temperature, -40°C ; vertical bars, cyclic pentamer (**5R**); cross-hatched, cyclic tetramer (**4R**).

measured on a JASCO A-3 spectrophotometer. NMR spectra were taken with JEOL JNM-MH-100 and JNM-FX-100 Fourier transform NMR spectrometers in deuteriochloroform or deuterioacetonitrile with tetramethylsilane as internal reference. Optical rotations were measured in chloroform at 25°C by using a JASCO DIP-4 automatic polarimeter and a 1-dm cell. The properties of the pure oligomers have been reported previously (**2**,¹⁸ **4**,¹⁸ **5**,¹⁸ **4R**,²¹ and **5R**²⁰).

Results and Discussion

Selective Formation of Optically Active Cyclic Tetramer 4R and Pentamer 5R from (+)-(1*R*,5*R*)-6,8-Dioxabicyclo[3.2.1]octan-7-one (1R). Figure 1 shows the time-conversion diagram for the oligomerization of **1R** in 1-nitropropane at -40°C , using boron trifluoride etherate as initiator. It is clearly demonstrated that the cyclic tetramer **4R** was preferentially formed in the early stage of the polymerization and that as the reaction proceeded, it was gradually converted to the cyclic pentamer **5R**, which was the sole product in the final stage. A similar trend was observed also in the oligomerization in chloroform and in acetonitrile, except that in the latter solvent, **4R** was obtained as a major product in a yield of nearly 30% in the middle stage of the reaction, and that even in the final stage, it was still obtained in a yield of about 20% along with the main product **5R**.²¹ Figure 2 illustrates a tail-biting mechanism for the formation of **4R** and **5R** from **1R**. The expression of configuration and conformation of the monomer and oligomers used throughout this paper is exemplified in the caption to Figure 2. For example, an ester oxygen on the extrapolated line connecting the acetal carbon and its neighboring methylene carbon signifies that the oxygen is in the axial position of the tetrahydropyran ring, while a carbonyl carbon on the line at right angles to the line connecting the carbonyl bearing methine carbon and its neighboring methylene carbon signifies that the carbonyl carbon is in the equatorial position. A main chain consisting of alternating ester and ether linkages is placed on a nearly flat plane, and the four C–C bonds connecting the carbons of a tetrahydropyran ring come either above the plane (a bold line) or below the plane (a dotted line). Taking such a spatial orientation of atoms into consideration, the absolute configuration (*R* or *S*) of the two asymmetric carbons of each monomeric unit can be determined as shown in the caption. An ester linkage connecting two tetrahydropyran rings takes the *trans* conformation because of steric hindrance between them.

As Figure 2 shows, a monomer (**2**) attacks the partially positively charged acetal carbon of the terminal oxonium ion (**1**) to invert its configuration (an alkyl-oxygen fission, as proved by the X-ray analysis of a **4R**-acetonitrile (1:1) complex²⁴), and simultaneously the flipping of the tetra-

Table I
Solubilities of Cyclic Oligomers of
6,8-Dioxabicyclo[3.2.1]octan-7-one^a

solvent	solubility, g/100 mL				
	2	4	5	4R	5R
CH ₃ CN	0.10	0.71	1.1	1.6	1.2
C ₂ H ₅ NO ₂	0.17	5.1	1.7	(8)	1.4
CHCl ₃	1.9	0.88	22	(45)	(9)

^a Temperature, -40 °C and (26 °C).

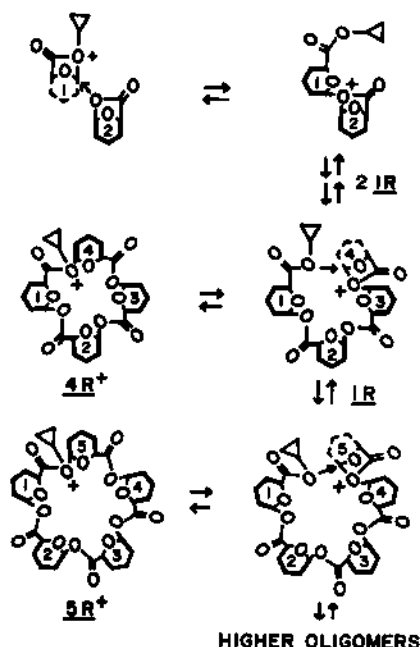
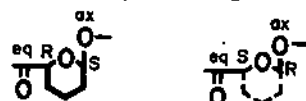


Figure 2. Mechanism of the formation of optically active cyclic tetramer (4R) and pentamer (5R) of (+)-(1R,5R)-6,8-dioxabicyclo[3.2.1]octan-7-one (1R) by tail-biting.



R, S: configuration of asymmetric atoms
ax, eq: conformation of substituent groups
Δ: initiator fragment

hydropyran ring of the ring-opened monomeric unit (1) occurs to give a conformation with its ester oxygen in the axial position and its carbonyl carbon in the equatorial position. As the middle formula on the right side in Figure 2 shows, the ester oxygen of the inactive terminal unit (1) attacks the partially positively charged acetal carbon of the active terminal unit (4) to form a cyclic tetramer oxonium ion (4R⁺) from which an initiator fragment is removed to provide 4R (tail-biting).

In a similar manner the cyclic pentamer 5R is also produced. One of the driving forces for these processes seems to be the crystallization of these cyclic oligomers due to their high molecular symmetry: 4R and 5R are chiral but not asymmetric molecules ("gyrochiral" molecules according to the definition proposed by Nakazaki et al.²⁵). These oligomers have C₄ and C₅ symmetry axes, respectively, and they are readily crystallized as expected. In contrast, conformationally highly strained gyrochiral dimer and trimer seem to be extremely unstable and, even if formed, would exist only transiently.

The transformation of once-formed 4R to 5R with reaction time and the predominant formation of 5R in the

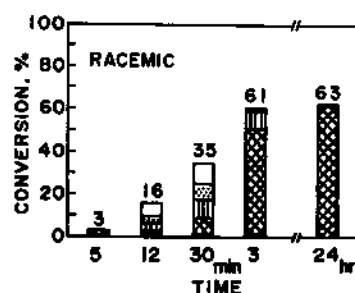


Figure 3. Time-conversion diagram for the oligomerization of racemic 6,8-dioxabicyclo[3.2.1]octan-7-one (1) in chloroform. Monomer, 1 g; chloroform, 1 mL; BF₃·OEt₂, 5 mol % to monomer; temperature, -40 °C; unshaded, polymer; dots, other oligomers; vertical bars, cyclic pentamer (5); cross-hatched, cyclic tetramer (4); shaded, cyclic dimer (2).

final stage of the reaction presumably arise from the lower solubility of 5R than that of 4R in the reaction media as shown in Table I and also from the lower conformational strain of 5R. In the oligomerization in acetonitrile, as described above, the formation of a 1:1 4R-acetonitrile complex seems to be responsible for the preferential formation of 4R, at least up to the middle stage of the reaction.

In the tail-biting mechanism shown in Figure 2, the transformation of 4R to 5R occurs via ring-chain equilibrium (cyclic oligomer-linear oligomer): 4R⁺ is ring-opened intramolecularly to give a linear tetramer oxonium ion, which in turn reacts with a monomer 1R, and subsequent ring closure by tail-biting leads to 5R⁺. Direct attack of 1R on 4R⁺ would give, via a linear pentamer oxonium ion and its tail-biting, an unsymmetrical cyclic pentamer. Actually, however, such a cyclic pentamer was not detected at all in the reaction mixture, and hence the reaction process involving direct attack of 1R on 4R⁺ can be excluded.

One might think that a ring-expansion mechanism proposed by Plesch and colleagues^{24,27} for the polymerization of cyclic acetals such as 1,3-dioxolane and 1,3-dioxepane can satisfactorily interpret the exclusive formation of cyclic oligomers in the present case. However, the mechanism cannot fully account for the selective formation of gyrochiral 4R and 5R and is also incompatible with the oligomerization behavior of racemic monomer which will be discussed in a later section.

Selective Formation of Cyclic Tetramer 4 and Cyclic Pentamer 5 from Racemic Monomer 1. In the cationic oligomerization of racemic monomer 1, there are two characteristic products which cannot be detected at all in the oligomerization of optically active monomer 1R under similar reaction conditions. One is a relatively high molecular weight polymer ($M_n \sim 10,000$ by GPC) formed in the initial stage of the reaction at temperatures below -40 °C, and the other is cyclic dimer 2, which is formed predominantly or nearly quantitatively in the final stage of reaction in acetonitrile and 1-nitropropane. The formation of 2 will be discussed separately in a later section.

Figure 3 shows the time-conversion diagram for the oligomerization of racemic monomer 1 in chloroform at -40 °C. In the early stage of the reaction, a polymer rather than oligomers was preferentially formed, and as the reaction proceeded, cyclic tetramer 4, cyclic pentamer 5, and other higher oligomers gradually accumulated. After 3 h most of the polymer and other higher oligomers were transformed to 4 and 5, and eventually the latter was completely converted to 4. Throughout the reaction, the formation of cyclic dimer 2 was negligible. Such an ex-

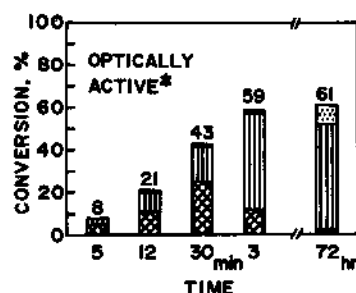


Figure 4. Time-conversion diagram for the oligomerization of optically active (+)-(1R,5R)-6,8-dioxabicyclo[3.2.1]octan-7-one (1R) in chloroform. Monomer, 1 g; chloroform, 1 mL; $\text{BF}_3 \cdot \text{OEt}_2$, 7 mol % to monomer; temperature, -40°C ; dots, other oligomers; vertical bars, cyclic pentamer (5R); cross-hatched, cyclic tetramer (4R).

Table II
Depolymerization of Cyclic Pentamer 5 and Polymer of 6,8-Dioxabicyclo[3.2.1]octan-7-one^a

	initial	
	5, ^b 1 g; CHCl_3 , 1 mL	polymer, ^c 0.9 g; CHCl_3 , 1.8 mL
final		
% polymer	0	6
% other oligomers	0	5
% 5	29	3
% 4	39	53
% 2	2	2
% 1	30	31
% total	100	100

^a Temperature, -40°C ; time, 3 days; $\text{BF}_3 \cdot \text{OEt}_2$, 10 mol % to monomer. ^b 5 fractionated by GPC from the oligomers obtained in the oligomerization of racemic 1 at -40°C in 1-nitropropane. ^c Polymer fractionated by GPC from the products obtained in the oligomerization of racemic 1 at -60°C in chloroform.

clusive formation of 4 is in remarkable contrast to the predominant formation of optically active cyclic pentamer 5R in the oligomerization of optically active monomer 1R under similar conditions.

The time-conversion diagram for the oligomerization of 1R in chloroform at -40°C is presented in Figure 4. Contrary to the oligomerization of racemic monomer 1, no polymer was formed even in the initial stage of the reaction. The optically active cyclic tetramer 4R once formed in the relatively early stage was transformed to the cyclic pentamer 5R, and after 3 days, 5R was obtained as the main product along with a small amount of other oligomers. The conversion from 4R to 5R in this case is indeed in the reverse direction to the conversion from 5 to 4 observed in the oligomerization of racemic monomer 1. Such peculiar and intriguing phenomena will be discussed later.

Table II presents the results of depolymerization of 5 at -40°C in 1-nitropropane and of a polymer obtained at -60°C in chloroform. It was confirmed that 5 and the polymer were transformed mainly to 4 and monomer 1 in chloroform at -40°C in the presence of boron trifluoride etherate, although the reaction was rather slow. This finding proves that 4 is formed also by the degradation of 5 and polymer.

Inspection of molecular models reveals that a growing chain entirely consisting of syndiotactic dyads ($-\text{R}-\text{S}-$) tends to form a linear polymer, while a growing chain entirely consisting of isotactic dyads ($-\text{R}-\text{R}-$ and $-\text{S}-\text{S}-$) can readily form a cyclic structure because of steric repulsion of the tetrahydropyran rings. (R and S denote 1R and 1S monomeric units, respectively.) Actually, X-ray

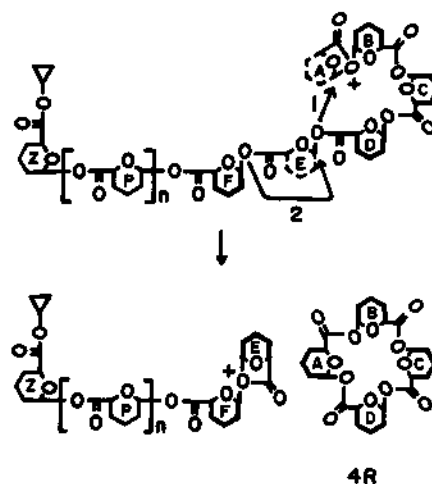


Figure 5. Mechanism of the formation of cyclic tetramer (4) of 6,8-dioxabicyclo[3.2.1]octan-7-one (1) by back-biting.

analysis of the crystals of the optically inactive cyclic tetramer 4 disclosed that it was not a meso compound (R-S-R-S) but a racemic mixture of 4R (R-R-R-R) and 4S (S-S-S-S).²⁸

Figure 5 shows a back-biting mechanism for the formation of 4 from the polymer. In the upper formula, A-B-C-D is an isotactic sequence of 1R (R-R-R-R), and D-E-F is a syndiotactic sequence of 1R-1S-1R (R-S-R). The ester oxygen of the monomer unit (D) attacks the activated acetal carbon of the terminal monomer unit (A) (arrow 1) to form a macrocyclic oxonium ion. Subsequently, the ester oxygen of the monomer unit (E) attacks its own acetal carbon (arrow 2) to liberate 4 (4R in this case). Depolymerization of the polymer to 1 also occurs. Such depolymerization of a growing chain or depolymerization followed by polymerization continues until an isotactic sequence of at least four identical enantiomeric units appears at the active chain end, from which 4 and 5 can be produced by back-biting.

The transformation from 5 to 4 in the oligomerization or racemic monomer in chloroform (Figure 3) is in the reverse direction to the transformation from 4R to 5R in the oligomerization of optically active monomer in the same solvent (Figure 4). Such a remarkable difference in the oligomerization behavior, which at first glance seems very strange, arises at least partly from the difference in the cyclization mechanism between the two systems; namely, 4R and 5R are produced by tail-biting, while 4 and 5 are produced chiefly by back-biting.

In the oligomerization of 1R, it is conceivable that a linear tetramer growing ion cyclizes by tail-biting to 4R faster than it propagates to a linear pentamer growing ion, which in turn cyclizes by tail-biting to 5R more readily than it propagates further. Thus, 4R is preferentially formed in the early stage of the reaction, but it is gradually converted to 5R by the mechanism depicted in Figure 2, since 5R is conformationally more stable than 4R.

In the oligomerization of racemic monomer, tail-biting cyclization to 4 and 5 is less likely to take place because there is a relatively small probability for a linear growing chain to consist of four or five identical enantiomeric units $\text{X}-\text{R}_{n-1}-\text{R}^+$ or $\text{X}-\text{S}_{n-1}-\text{S}^+$ ($n = 4$ or 5 ; X = initiator fragment). After the polymerization has proceeded to middle or later stages, where polymerization-depolymerization equilibrium becomes significant, sequences of the same enantiomeric units would be formed at a growing chain end, from which 4 or 5 is produced by back-biting. In view of the finding that comparable amounts of 4 and 5 are

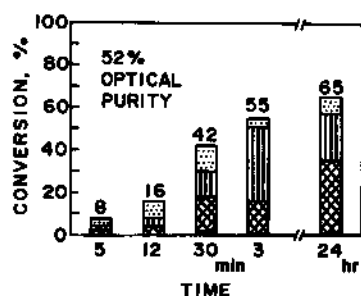


Figure 6. Time-conversion diagram for the oligomerization of optically active 6,8-dioxabicyclo[3.2.1]octan-7-one of 52% optical purity in chloroform. Monomer, 2 g; chloroform, 2 mL; $\text{BF}_3 \cdot \text{OEt}_2$, 5 mol % to monomer; temperature -40°C ; dots, other oligomers; vertical bars, cyclic pentamer; cross-hatched, cyclic tetramer; shaded, cyclic dimer.

Table III
Variation of Specific Rotation of Residual Monomer, Cyclic Tetramer, and Cyclic Pentamer in the Oligomerization of 6,8-Dioxabicyclo[3.2.1]octan-7-one of 52% Optical Purity^a

time	conversion, %	$[\alpha]_D^{25}$, deg		
		monomer	tetramer	pentamer
5 min	8	+68 (3.2) ^c		
12 min	16	+62 (2.7) ^c	-144	-56
30 min	42	+51 (2.3) ^c	-145	-64
3 h	55	+44 (2.1) ^c	-59	-105
24 h	65	+72 (3.4) ^c	-9	-108

^a Monomer ([1R]/[1S] = 3.2), 2 g; chloroform, 2 mL; $\text{BF}_3 \cdot \text{OEt}_2$, 5 mol % to monomer; temperature, -40°C .

^b $[\alpha]_D^{25}$ (chloroform, 1%): 1R, $+130^\circ$; 4R, -168° ; 5R, -112° . ^c Figures in parentheses denote the enantiomer ratio [1R]/[1S].

produced up to the middle stage of the polymerization, the rate of back-biting of a growing chain end having four consecutive same enantiomeric units to 4 may be lower than, or at most nearly equal to, the rate of propagation.

The difference in the reactivity of a growing chain end between tail-biting and back-biting seems to arise from the fact that the former involves the attack of an active chain end at the ester oxygen of a carboxyl or ethoxycarbonyl end group, while the latter involves the attack of an active chain end at the ester oxygen of an inner chain unit. Because of steric crowding, such a back-biting reaction undoubtedly requires a higher activation energy than tail-biting.

In order to further clarify the cause for the remarkable difference in the oligomerization behavior between racemic monomer 1 and optically active 1R as described above, the oligomerization of enantiomerically unbalanced monomer mixtures was undertaken under similar reaction conditions. Figure 6 shows the time-conversion diagram of the oligomerization of a monomer mixture of 52% optical purity (1R/1S = 3.2). Table III summarizes the variation of specific rotation of residual monomer, cyclic tetramer, and cyclic pentamer with conversion. In the early and middle stages of the reaction, the specific rotation of the cyclic tetramer was close to that of pure 4R (-168°) obtained from 1R. Therefore, it is highly probable that this cyclic tetramer was formed by a tail-biting reaction as the formation of 4R in the oligomerization of 1R (Figure 2). However, the specific rotation of cyclic tetramer became significantly less negative with increasing reaction time, and after 1 day it was as low as -9° . The formation of the practically optically inactive cyclic tetramer in the later stage of the reaction seems to indicate that it was

formed primarily by a back-biting reaction from 5 or other oligomers as the formation of 4 in the oligomerization of racemic monomer 1 (Figure 5). On the contrary, the specific rotation of cyclic pentamer changed from -56 to -108° with reaction time. The latter value was very close to that of pure 5R (-112°) obtained from 1R, suggesting that the cyclic pentamer in the later stage of the reaction was formed mainly from 4R through the process proposed in the previous section for the selective formation of 5R in the oligomerization of 1R (Figure 2).

The specific rotation of residual monomer, on the other hand, decreased with reaction time and it became $+44^\circ$ ([1R]/[1S] = 2.1) after 3 h. This means that the 1R enantiomer, being in excess, was preferentially converted to cyclic oligomers; in other words, the preferential selection of the monomer of the same chirality as that of the terminal unit of the growing chain occurred in this reaction. Such stereoregulation was found in the cationic polymerization of 6,8-dioxabicyclo[3.2.1]octane at low temperatures.²⁰ After 24 h, however, the specific rotation of the residual monomer increased to nearly the same value as that of the starting monomer ([1R]/[1S] = 3.2), although the total conversion to cyclic oligomers did not increase appreciably. This is probably due to a thermodynamic equilibrium between monomer and cyclic oligomers. In the final stage, and therefore presumably in an equilibrium state, nearly half of the total products was optically inactive cyclic tetramer 4 and the other half was optically active cyclic pentamer 5R plus some other oligomers. Furthermore, a similar phenomenon was observed in the oligomerization of a monomer mixture of 35% optical purity ([1R]/[1S] = 2.1): In the later stage of the reaction, about two-thirds of the total products was 4 and the remaining third was mainly 5R. These results are closely related to the selective formation of 5R from 1R of 100% optical purity and of 4 from 1 of 0% optical purity in chloroform at -40°C . Such a characteristic product distribution depending on the optical purity of monomer can be interpreted as follows: In view of the fact that 4 is an equimolar mixture of 4R and 4S which form a racemate crystal as proved by X-ray analysis,²⁰ it seems very likely that in the oligomerization of 1 in chloroform, 4R is stabilized only when it can interact with its counterpart 4S to precipitate out of the solution. On the contrary, in the absence of 4S or in the presence of a smaller amount of 4S, 4R, being in excess, is transformed to more stable 5R. This is supported by the facts that the solubility of 4 in chloroform is much lower than that of 4R in the same solvent (Table I) and that 4 is readily crystallizable in chloroform, while 4R is not. The preferential formation of 5, instead of 4, in the oligomerization of 1 in 1-nitropropane suggests that such stabilization of 4 by an interaction between its enantiomer pair is not strong enough to suppress the transformation of 4 to 5 in solvents of higher polarity, such as 1-nitropropane.

Formation of Cyclic Dimer 2 from Racemic Monomer 1. The cyclic dimer 2 consists of a pair of different enantiomers of 1, and all four substituents attached to the two tetrahydropyran rings are axially oriented.²⁴ Therefore, the fact that no cyclic dimer is formed in the oligomerization of optically active 1R is quite reasonable. Furthermore, the possibility that the cyclic dimer 2 polymerizes to afford selectively the cyclic oligomer 4 is definitely excluded because 2, consisting of a pair of 1R and 1S monomeric units, cannot be converted, by any simple mechanism, directly to 4, which is a racemic mixture of 4R and 4S. In addition, the fact that the ester oxygen and carbonyl carbon of each monomeric unit in 4

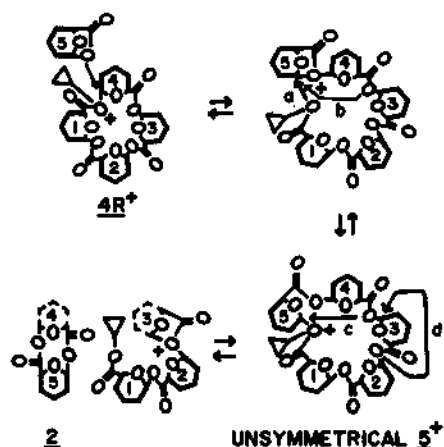


Figure 7. Mechanism of the formation of cyclic dimer (2) of 6,8-dioxabicyclo[3.2.1]octan-7-one (1) by the reaction of cyclic tetramer with monomer.

are located in axial and equatorial positions of the tetrahydropyran ring, respectively, is further evidence against the possibility described above.

There are at least two experimental findings which would provide useful information on the mechanism of the formation of 2. First, 2 was hardly produced in the initial stage of the oligomerization of 1, where 4 and 5 were preferentially formed, but it was produced highly selectively in the final stage of reaction, except in chloroform. Second, as revealed by X-ray analysis,²⁴ the configuration of all the acetal carbons of 4R is inverted compared with that of the acetal carbon of 1R; in other words, the oligomerization proceeds via an S_N2 -type mechanism with an exclusive alkyl-oxygen bond fission of 1R. In view of these facts, it seems reasonable that 2 is formed by the reaction of cyclic oligomer with monomer.

Figure 7 illustrates a possible mechanism for the formation of 2 by intramolecular reaction of unsymmetrical oligomer 5^+ , which is formed by the reaction of $4R^+$ with 1S: The activated acetal carbon of the monomeric unit (4) of $4R^+$ is attacked by the ester oxygen of 1S (5) to give a linear oxonium ion with the inversion of the configuration of the acetal carbon of the monomeric unit (4) from S to R. Then the acetal carbon of the terminal oxonium ion (5) is attacked by the ester oxygen of monomeric unit (1) (arrow a) to give unsymmetrical cyclic pentamer oxonium ion (unsymmetrical 5^+). This oxonium ion seems to exist only transiently because of its unstability due to the unsymmetrical structure. Thus, intramolecular reaction of the ester oxygen of the monomeric unit (4) with the partially positively charged acetal carbon of the monomeric unit (5) (arrow c) takes place to give a linear pentamer having a cyclic dimer oxonium ion at its end. It seems likely that this reaction is accompanied by flipping of the tetrahydropyran ring (4) since it allows its ester oxygen to come near the acetal carbon of the monomeric unit (5). Subsequent attack of the ester oxygen of the monomeric unit (3) to its partially positively charged acetal carbon (arrow d) occurs to liberate 2, which consists of a pair of different enantiomers (1R (4) and 1S (5)) and has all four substituents in the axial positions of the tetrahydropyran ring.

Direct back-biting from a linear oxonium ion can be ruled out. For example, in the upper formula on the right side, intramolecular reaction of the ester oxygen of the monomeric unit (4) with the acetal carbon of the linear pentamer oxonium ion (5) (arrow b) would lead to a cyclic dimer in which three substituents are equatorially oriented and one substituent is axially oriented (or vice versa).

However, cyclic dimer having such a configuration was not detected at all in the present oligomerization.

In comparison with 4R and 5R, which are chiral but not asymmetric molecules (gyrochiral molecules), the cyclic dimer (2) is a symmetric molecule having a center of symmetry and it is more readily crystallized. In fact, among the three cyclic oligomers (2, 4, and 5), 2 has the lowest solubility in acetonitrile and 1-nitropropane, as shown in Table II. Therefore, as in the selective formation of cyclic tetramer and pentamer, solubility and molecular symmetry also play an important role in the formation of 2.

Conclusion

The aforementioned results and discussion lead us to the following conclusions as to the mechanisms of the selective formation of the 10-, 20-, and 25-membered macrocyclic oligoesters.

(1) In the oligomerization of optically active monomer 1R, the optically active cyclic tetramer 4R and cyclic pentamer 5R are formed by a tail-biting reaction of a growing oligomer chain.

(2) In the oligomerization of racemic monomer 1, on the other hand, the racemic cyclic tetramer 4 and cyclic pentamer 5 are produced mainly by a back-biting reaction of a growing polymer chain.

(3) The cyclic dimer 2, which is obtained only in the oligomerization of racemic monomer 1 in acetonitrile and 1-nitropropane, is formed primarily by intramolecular reaction of unsymmetrical cyclic oligomers which are formed by the reaction between cyclic oligomers and monomer.

(4) All these macrocyclic oligoesters are formed via an S_N2 -type mechanism involving the exclusive alkyl-oxygen fission of 1.

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References and Notes

- Goethals, E. J. *Adv. Polym. Sci.* 1977, 23, 103.
- Jacobson, H.; Stockmayer, W. H. *J. Chem. Phys.* 1950, 18, 1600.
- Semlyen, J. A. *Adv. Polym. Sci.* 1976, 21, 41.
- Ito, K.; Hashizuka, Y.; Yamashita, Y. *Macromolecules* 1977, 10, 821.
- Rentah, C.; Schulz, R. C. *Makromol. Chem.* 1978, 179, 1403.
- Flory, P. J.; Semlyen, J. A. *J. Am. Chem. Soc.* 1966, 88, 3209.
- Flory, P. J.; Suter, U. W.; Mutter, M. *J. Am. Chem. Soc.* 1976, 98, 5733.
- Suter, U. W.; Mutter, M.; Flory, P. J. *J. Am. Chem. Soc.* 1976, 98, 5740.
- Mutter, M.; Suter, U. W.; Flory, P. J. *J. Am. Chem. Soc.* 1976, 98, 5745.
- Matyjaszewski, K.; Zielinski, M.; Kubisa, P.; Stomkowski, S.; Chojnowski, J.; Penczek, S. *Makromol. Chem.* 1980, 181, 1469.
- (a) Tsuboyama, S.; Tsuboyama, K.; Higashi, I.; Yanagita, M. *Tetrahedron Lett.* 1970, 16, 1367. (b) Tsuboyama, K.; Tsuboyama, S.; Uzawa, J.; Higashi, I. *Chem. Lett.* 1974, 1367.
- Sato, A.; Hirano, T.; Suga, M.; Tsuruta, T. *Polym. J.* 1977, 9, 209.
- (a) Dreyfuss, P.; Dreyfuss, M. P. *Polym. J.* 1976, 8, 81. (b) Bucquoye, M. R.; Goethals, E. J. *Makromol. Chem.* 1979, 179, 1681. (c) Bucquoye, M. R.; Goethals, E. J. *Polym. Bull.* 1980, 2, 702.
- Dale, J.; Borgen, G.; Daasvatn, K. *Acta Chem. Scand., Ser. B* 1974, 28, 378.
- Dale, J.; Daasvatn, K. *J. Chem. Soc., Chem. Commun.* 1976, 295.
- Dale, J.; Daasvatn, K.; Gronneberg, T. *Makromol. Chem.* 1977, 178, 873.
- Okada, M.; Sumitomo, H.; Yamamoto, Y. *Makromol. Chem.* 1974, 175, 3023.

- (18) Okada, M.; Sumitomo, H.; Tajima, I. *Macromolecules* 1977, 10, 505.
- (19) Okada, M.; Sumitomo, H.; Tajima, I. *Polym. Bull.* 1978, 1, 41.
- (20) Okada, M.; Sumitomo, H.; Tajima, I. *J. Am. Chem. Soc.* 1979, 101, 4013.
- (21) Tajima, I.; Okada, M.; Sumitomo, H. *Makromol. Chem. Rapid Commun.* 1980 1, 197.
- (22) In the previous papers,¹⁷⁻²¹ it was erroneously reported that a 30-membered cyclic hexamer was produced from both racemic and optically active 6,8-dioxabicyclo[3.2.1]octan-7-ones on the basis of the molecular weight determination by vapor pressure osmometry. Recent X-ray analysis has disclosed that it is actually a 25-membered cyclic pentamer. The error was due to the formation of a 1:1 molecular complex of the cyclic pentamer with chloroform, whose molecular weight was close to that of the cyclic hexamer.
- (23) Lehninger, A. L. "Biochemistry"; Worth Publishers: New York, 1970; p 614.
- (24) Tanaka, I.; Tajima, I.; Hayakawa, Y.; Okada, M.; Bitoh, M.; Ashida, T.; Sumitomo, H. *J. Am. Chem. Soc.* 1980, 102, 7873.
- (25) Nakazaki, M.; Naemura, K.; Yoshihara, H. *Bull. Chem. Soc. Jpn.* 1975, 48, 3278.
- (26) Plesch, P. H.; Westermann, P. H. *J. Polym. Sci., Part C* 1968, 16, 3837.
- (27) Plesch, P. H.; Westermann, P. H. *Polymer* 1969, 10, 105.
- (28) Ashida, T., et al., to be submitted for publication.
- (29) Okada, M.; Sumitomo, H.; Komada, H. *Macromolecules* 1979, 12, 395.