Macromolecules 1986, *19*, 953-959

Synthesis and Ring-Opening Polymerization of Bicyclic Lactones Containing a Tetrahydropyran Ring.
2,5-Dioxabicyclo[2.2.2]octan-3-one

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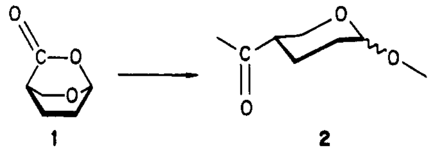
Received September 19, 1985

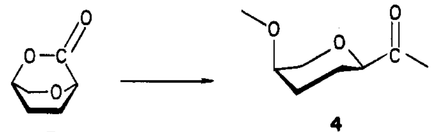
ABSTRACT: A new bicyclic lactone, 2,5-dioxabicyclo[2.2.2]octan-3-one (3), was synthesized from sodium 3,4-dihydro-2*H*-pyran-2-carboxylate (5) by esterification, hydroboration followed by oxidation to the corresponding alcohol, and subsequent acid-catalyzed intramolecular transesterification. The overall yield was approximately 20%. Polymerization of 3 was attempted under a variety of reaction conditions. Trifluoromethanesulfonic acid initiated the polymerization of 3, whereas Lewis acids were totally ineffective. Anionic and coordination initiators such as lithium benzophenone ketyl, butyllithium, and tetraisopropyl titanate induced the polymerization of 3 to afford white powdery polymers having number-average molecular weights of (2-9) × 10^3 and relatively broad molecular weight distributions. A fractionated polymer with a number-average molecular weight of 1.4 × 10^4 melted at 281-297 °C (DSC) and dissolved in dichloromethane, chloroform, and hot γ-butyrolactone. ^{13}C NMR analysis showed that the polymer was polyester 4, entirely consisting of cis-2,5-linked tetrahydropyran rings. The polymerization reactivity of 3 is discussed.

Introduction

Tetrahydropyran rings are very common in naturally occurring structures such as polysaccharides and antibiotics. In a previous paper,[1] we reported the first synthesis of a strained bicyclic lactone, 2,6-dioxabicyclo[2.2.2]octan-3-one (1), from acrolein and dimethyl malonate and its ring-opening polymerization to high molecular weight polyester 2 containing tetrahydropyran rings in the main chain. As a continuation of a series of works on the synthesis of oxacyclic polymers of potential biomedical utility, we have undertaken the synthesis and polymerization of 2,5-dioxabicyclo[2.2.2]octan-3-one (3) and its polymerization to polyester 4. Since polyesters 2 and 4 seem to be hydrolyzed under physiological conditions, it is hoped that they are applicable as biodegradable slow-release agents and surgical sutures.



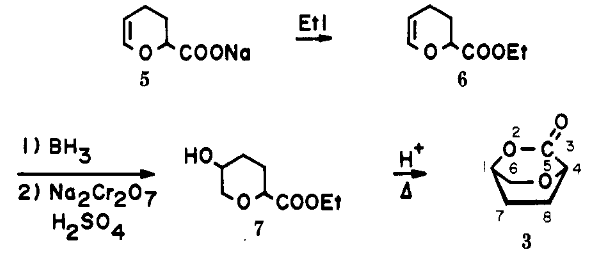
(1)



(2)

Bicyclic lactone 1 can be regarded as a bicyclic acetal-ester, and in fact it was very readily polymerized with cationic initiators.[1] Particularly, boron trifluoride etherate was effective for the formation of high molecular weight polyester. The cationic polymerization of 1 proceeds through the C(1)-O(2) bond cleavage (alkyl-oxygen scission) of its oxonium ion aided by the stabilization of an incipient positive charge on the C(1) atom by the adjacent O(6) atom. However, the resulting polymer was composed of not only trans-disubstituted tetrahydropyran units but also the cis counterparts, their proportions being variable depending on the reaction conditions. The structural irregularity of the polymer conceivably arises from transacetalization during polymerization, although S_N1-type propagation by an oxacarbenium ion giving both the cis and trans structural units may contribute to some extent.

Scheme I
Synthetic Route of 2,5-Dioxabicyclo[2.2.2]octan-3-one (3)



Bicyclic lactone 3 does not contain any acetal linkage, and consequently its cationic polymerizability should be reduced significantly compared with that of 1. Rather, polymerization of 3 would be more readily initiated with anionic initiators to give polyester 4 through the acyl-oxygen scission of the ester linkage. Since transesterification, even if it occurs, does not affect the structure of the polymer, it is expected that structurally regular polyester entirely consisting of cis-2,5-linked tetrahydropyran units will be formed in the anionic polymerization of 3. The present paper describes the synthesis of bicyclic lactone 3 and its ring-opening polymerization to polyester 4 containing tetrahydropyran rings in the main chain.

Results and Discussion

Synthesis. 2,5-Dioxabicyclo[2.2.2]octan-3-one (3) was synthesized from sodium 3,4-dihydro-2*H*-pyran-2-carboxylate (5) as illustrated in Scheme I. Sodium salt 5 was esterified with ethyl iodide in dimethylformamide to afford ethyl 3,4-dihydro-2*H*-pyran-2-carboxylate (6). Hydroboration of 6 with a borane solution in tetrahydropyran[2] at 0 °C, followed by oxidation with an aqueous sodium dichromate-sulfuric acid solution and subsequent treatment with sodium hydrogen sulfite gave ethyl 5-hydroxytetrahydropyran-2-carboxylate (7) as a stereoisomeric mixture (cis:trans = 1:~1). The hydroxytetrahydropyran ester 7 was heated in a dilute solution in the

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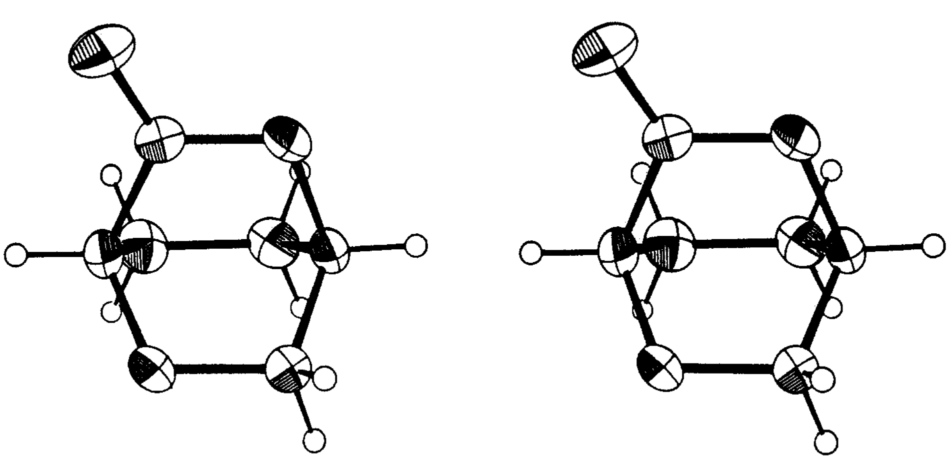


Figure 1. Stereodrawing of 2,5-dioxabicyclo[2.2.2]octan-3-one (3). The thermal ellipsoids are drawn at the 50% probability level.

presence of a catalytic amount of *p*-toluenesulfonic acid. Liberated ethyl alcohol was removed through a Soxhlet extractor containing molecular sieves 5A. Column chromatographic separation of the reaction products and subsequent repeated recrystallization gave the bicyclic lactone **3** as colorless crystals. The overall yield of **3** based on **5** was approximately 20%.

Sodium dichromate–sulfuric acid oxidation has been used to convert alkylboranes to ketones.[3] Actually, when the reaction mixutre of the sodium dichromate–sulfuric acid oxidation above was worked up without treatment with sodium hydrogen bisulfite, ethyl 5-oxotetrahydropyran-2-carboxylate was obtained as a major product instead of **7**. The keto compound on reduction with sodium borohydride in methanol afforded **7** as a mixture of the cis and trans isomers (1:~2).

In preliminary experiments, we found that the hydroboration of **6** followed by oxidation with 30% aqueous hydrogen peroxide in the presence of sodium acetate at 0 °C gave rise to **7** predominantly composed of the trans isomer (cis:trans = 1:>5).[4] Since only the cis isomer undergoes intramolecular transesterification to give the bicyclic lactone **3**, we attempted several reactions to convert the trans isomer of **7** to the cis counterpart, but none were successful. For instance, tosylation of **7** followed by nucleophilic substitution with tetraethylammonium bromide led to the corresponding bromide with the inverted configuration of the C(5) atom. The bromo ester was then transformed to the silver carboxylate, but its cyclization by heating at 140–150 °C under vacuum[5] was unsuccessful. A promising method to invert the configuration of the carbon atom bearing the hydroxyl group in **7** is to treat its tosylate or mesylate with potassium superoxide.[6-9] Unexpectedly, however, a violent explosion occurred when potassium superoxide powder was added to a solution of the mesylate of **7** in a mixture of dimethoxyethane and dimethyl sulfoxide under an argon atmosphere. Therefore, this method was abandoned.

The bicyclic lactone **3** was prepared also by heating 5-hydroxytetrahydropyran-2-carboxylic acid at 200–210 °C under vacuum without using solvent and catalyst. However, this method gave poor reproducibility and a lower yield of **3** compared with the bicyclization of **7** in a dilute toluene solution described above.

The bicyclic lactone **3** existed as hygroscopic crystals melting at 56–57 °C. Table I summarizes bond lengths and bond angles for **3**. Figure 1 depicts a stereodrawing of **3**. Unlike 2,6-dioxabicyclo[2.2.2]octan-3-one,[1] the two C–O bonds (C(4)–O(5) and C(6)–O(5)) of the tetrahydropyran ring in **3** are symmetrical. The C(1)–C(6) bond (1.495 Å) is considerably shorter than the ordinary C–C bond (1.54 Å).

Table I
Bond Lengths (Å) and Bond Angles (Deg) for 2,5-Dioxabicyclo[2.2.2]octan-3-one (3)[a]

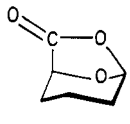
	Bond Lengths		
O(5)–C(4)	1.431 (1)	C(4)–C(3)	1.505 (1)
O(5)–C(6)	1.429 (1)	C(4)–C(8)	1.513 (1)
O(2)–C(3)	1.341 (1)	C(1)–C(6)	1.495 (1)
O(2)–C(1)	1.463 (1)	C(1)–C(7)	1.509 (1)
O(9)–C(3)	1.198 (1)	C(7)–C(8)	1.525 (2)
	Bond Angles		
C(4)–C(5)–C(6)	111.63 (7)	O(9)–C(3)–C(4)	126.9 (1)
C(3)–O(2)–C(1)	111.93 (7)	O(2)–C(1)–C(6)	106.95 (8)
O(5)–C(4)–C(3)	108.23 (8)	O(2)–C(1)–C(7)	107.93 (8)
O(5)–C(4)–C(8)	109.99 (9)	C(6)–C(1)–C(7)	111.48 (9)
C(3)–C(4)–C(8)	107.97 (9)	O(5)–C(6)–C(1)	109.37 (8)
O(2)–C(3)–O(9)	121.00 (9)	C(1)–C(7)–C(8)	108.29 (9)
O(2)–C(3)–C(4)	112.14 (8)	C(4)–C(8)–C(7)	107.59 (9)

[a] Numbers in parentheses are estimated standard deviations in the least significant digits.

Polymerization. Polymerization of **3** was carried out under a wide variety of reaction conditions. Some of the results are listed in Table II.

Lewis acids such as antimony pentachloride, phosphorus pentafluoride, and boron trifluoride etherate were totally ineffective in initiating the polymerization of **3**. Trifluoromethanesulfonic acid induced the polymerization of **3**, but the yield and molecular weight of the polymer were low. This result is in marked contrast to the polymerization of **1**, which undergoes cationic polymerization very rapidly to afford high molecular weight polyester.[1]

Rate constants of acid-catalyzed hydrolysis may be taken as a measure of reactivity in cationic ring-opening polymerization of bicyclic monomers. For example, Hall et al.[10-12] determined the rate constants of acid-catalyzed hydrolysis of several bicyclic acetals with different skeletons by NMR spectroscopy, and they correlated the relative reactivities spanning more than five powers of ten with ring strain and Eliel's "rabbit-ear" effects. In a similar manner, the rates of dichloroacetic acid catalyzed hydrolysis of bicyclic lactones were measured in a mixture of deuterioacetone and deuterium oxide (4:1 (v/v)) at 25 °C. In accordance with the poor cationic polymerizability, **3** was not hydrolyzed to a detectable extent, whereas **1**, 6,8-dioxabicyclo[3.2.1]octan-7-one (**8**), and ϵ-caprolactone as a reference compound were hydrolyzed under the identical conditions to give first-order rate constants of 5.6×10^{-5}, 1.6×10^{-5}, and 0.4×10^{-5} s^{-1}, respectively. These data are in conformity with the high reactivity in cationic polymerization of **1** and **8**.[1,13-15]



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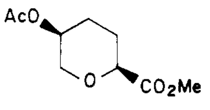
The bicyclic lactone **3** was polymerized with anionic and coordination initiators such as butyllithium, lithium benzophenone ketyl, and tetraisopropyl titanate. However, the yields and number-average molecular weights of the polymers were quite low. The unexpectedly low yields and low molecular weights of the polymers arise, at least partly, from the precipitation of the polymer from tetrahydrofuran or toluene solution during polymerization, in other words, the occlusion of the growing species. In fact, the polymer was insoluble in common organic solvents except dichloromethane and chloroform at room temperature.

A notable feature of the polymer thus obtained is its high melting point. A fractionated polymer having a number-average molecular weight of 1.4×10^4 melted at 281–297 °C (DSC), approximately 140 °C higher than the high molecular weight polyester **2** derived from the isomeric bicyclic lactone **1**.[1] Such a high melting point strongly suggests a higher structural regularity of the polymer. As will be described below, this polymer is entirely composed of cis-disubstituted tetrahydropyran units and is structurally homogeneous, whereas **2** contains both trans- and cis-disubstituted tetrahydropyran units and is structurally less regular. In addition, **2** comprises thermally unstable ester–acetal structures and it melts with decomposition.[1] On the other hand, the polymer derived from the bicyclic lactone **3** does not decompose, at least up to 300 °C. In connection with the high melting point, this polymer showed crystalline peaks in its X-ray diffraction pattern even in a powdery state. The elemental analytical data for the polymer were satisfactory.

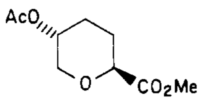
Structure and Stereochemistry. Figures 2 and 3 show the ^{1}H and ^{13}C NMR spectra of the polymer prepared in tetrahydrofuran at 0 °C with lithium benzophenone ketyl as the initiator, along with the assignments of the signals.[16] In the ^{1}H NMR spectrum, signal d at δ 3.68 appears as a doublet with a coupling constant of 12 Hz. This signal is informative of the structure of the polymer as will be shown below.

In the ^{13}C NMR spectrum, the appearance of a set of six distinct signals suggests that the polymer is structurally homogeneous. However, it is to be noted here that signal d, assignable to the methine carbon atom linked to the exocyclic oxygen atom, consists of two peaks with slightly different chemical shifts (δ 67.25 and 67.06). A similar phenomenon was previously observed in the ^{13}C NMR spectrum of the polyester derived from 6,8-dioxabicyclo[3.2.1]octan-7-one.[14] Since the bicyclic lactone **3** is racemic, the splitting of signal d is presumably due to different diad placements of the enantiomeric monomeric units in the polymer chain, as proved in the cases of polyacetals from 6,8-dioxabicyclo[3.2.1]octanes.[17]

In order to determine the stereochemical structure of the polymer, cis and trans isomers of methyl 5-acetoxytetrahydropyran-2-carboxylate (**9**) were prepared as model



9, cis



9, trans

compounds for the polymer, and their ^{1}H and ^{13}C NMR data were compared with those for the polymer. For the cis isomer, the axial proton of the methylene group adjacent to the ring oxygen in the 2e/5a form (see eq 3) exhibits doublet–doublet signals centered at δ 3.69 (3.72_7, 3.71_5, 3.66_4, and 3.65_4) with coupling constants of 2.1 and 12.3 Hz. For the trans isomer, the corresponding proton shows doublet–doublet signals centered at δ 3.37 (3.42_5, 3.38_0, 3.36_8, and 3.32_4) with coupling constants of 8.8 and 11.2 Hz.

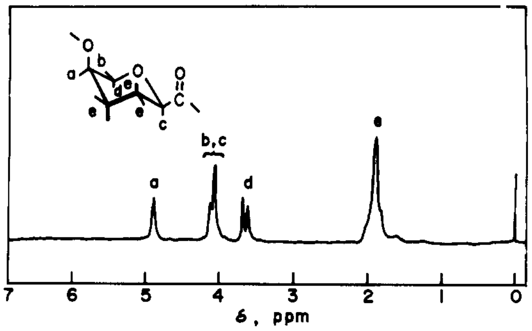


Figure 2. ^{1}H NMR spectrum of poly(tetrahydropyran-2,5-diyloxycarbonyl) prepared in tetrahydrofuran at 0 °C with lithium benzophenone ketyl as the initiator. Solvent, $CDCl_3$; temperature, 50 °C; 200 MHz; internal reference, tetramethylsilane.

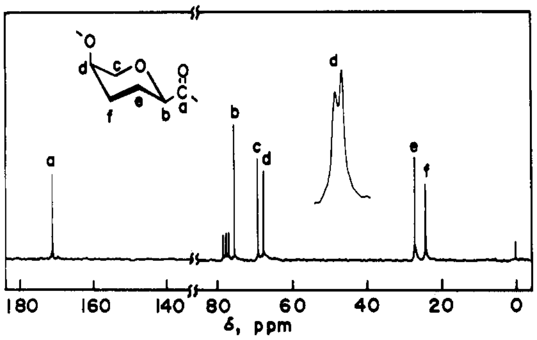


Figure 3. ^{13}C NMR spectrum of poly(tetrahydropyran-2,5-diyloxycarbonyl) prepared in tetrahydrofuran at 0 °C with lithium benzophenone ketyl as the initiator. Solvent, $CDCl_3$; temperature, 50 °C; 50 MHz; internal reference, tetramethylsilane.

Because of lower resolution in the ^{1}H NMR spectrum of the polymer, the corresponding proton in the polymer would appear as doublet signals for the cis unit and triplet signals for the trans unit. In fact, signal c, assignable to the axial proton of the methylene group adjacent to the ring oxygen in the repeating unit, appears as a doublet at δ 3.68 with a coupling constant of 12 Hz (Figure 2). Therefore, this is strongly indicative of the cis-2,5-linked tetrahydropyran structure (**4**) of the repeating unit in the polymer.

As for the ^{13}C NMR spectra, the chemical shifts of the respective carbons for the polymer, especially those of C(3) and C(4) (signals e and f), agreed with those of the corresponding carbons for the cis isomer of **9** (Table III), indicating again that the polymer consisted of the cis unit. Furthermore, the cis structure was also supported by comparison of the ^{13}C NMR chemical shifts of a terminal unit carrying a hydroxyl group of a low molecular weight polymer with those of the cis and trans isomers of methyl 5-hydroxytetrahydropyran-2-carboxylate. The chemical shifts of the terminal unit also agreed well with those of the cis isomer rather than those of the trans isomer (Table III).

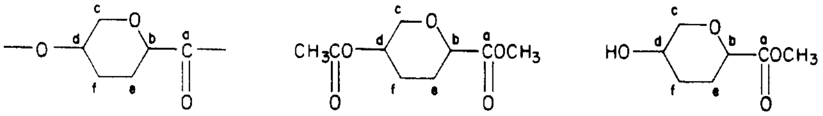
The cis-disubstituted tetrahydropyran unit in the polymer chain may take two conformations: One has the 2-equatorial and 5-axial substituents, and the other has the 2-axial and 5-equatorial substituents. These two conformers are probably in rapid equilibrium with each other. In order to estimate the proportion of these two

Table II
Polymerization of 2,5-Dioxabicyclo[2.2.2]octan-3-one (3)

amt of monomer, g	solvent[a] (mL)	initiator[b] (mol %)	temp, °C	time, h	yield,[c] %	$M_n \times 10^{-3}$ [d]	M_w/M_n
0.64	DCM (2.0)	CF_3SO_3H (5)	0	46	44	4.0	1.1
1.0	DCM (1.0)	$SbCl_5$ (5)	−60	8	0		
0.31	DCM (1.0)	PF_5 (4)	−60	70	0		
0.50	DCM (0.5)	BF_3OEt_2 (5)	−78	24	0		
0.64	THF (2.0)	Li-BzPh (0.8)	40	6	41	7.3	3.7
0.64	THF (2.0)	Li-BzPh (0.8)	20	30	47	8.2	4.2
0.64	THF (3.0)	Li-BzPh (0.8)	0	6	15	4.3	1.6
0.64	THF (3.0)	Li-BzPh (0.8)	0	100	29	8.9	3.9
1.94	THF (8.0)	Li-BzPh (1.6)	0	40	51	7.6	2.8
0.64	TOL (2.0)	n-BuLi (5)	0	20	30	3.4	1.3
0.77	TOL (3.0)	$Ti(OiPr)_4$ (1.0)	80	24	7		
0.77	bulk	$Ti(OiPr)_4$ (1.0)	60	5	46	2.5[e]	1.2
0.77	bulk	$Ti(OiPr)_4$ (0.2)	60	30	8		

[a] DCM, dichloromethane; TOL, toluene; THF, tetrahydrofuran. [b] Li-BzPh, lithium benzophenone ketyl. [c] Methanol-insoluble polymer. [d] By gel permeation chromatography (polystyrene standard). [e] By ^{1}H NMR spectroscopy.

Table III
^{13}C NMR Chemical Shifts for Poly(tetrahydropyran-2,5-diyloxycarbonyl) and Its Model Compounds[a]

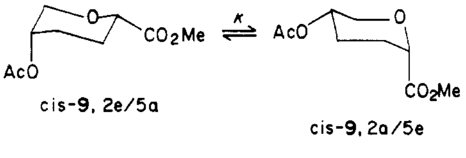


polymer MAPC MHPC

	assignment					
	a	b	c	d	e	f
polymer	169.94	75.12	68.88	67.25[b] 67.06[b]	26.98	24.01
		(75.52)[c]	(71.93)[c]	(64.09)[c]	(29.47)[c]	(23.88)[c]
MAPC[d]						
cis isomer	170.86	75.26	68.95	66.57	26.90	24.03
trans isomer	170.84	74.99	68.29	67.03	27.75	26.35
MHPC[e]						
cis isomer	171.64	75.41	71.76	63.80	29.38	23.60
trans isomer	171.30	75.31	71.98	64.89	31.61	27.76

[a] Solvent, $CDCl_3$; 200 MHz; internal reference, tetramethylsilane; δ in ppm. [b] The appearance of a pair of signals may be ascribable to different diad placements of the D,L-enantiomeric units in a polymer chain. [c] Chemical shifts for a terminal unit of a low molecular weight polymer prepared with n-butyllithium as the initiator. [d] Methyl 5-acetoxytetrahydropyran-2-carboxylate. [e] Methyl 5-hydroxytetrahydropyran-2-carboxylate.

conformers, the conformational free energy difference ΔG between the two conformers of the cis isomer of **9** was calculated. The conformational free energy parameters of substituents in tetrahydropyrans employed for the calculation were as follows (in kJ/mol): 2-CO_2Me, 5.78[18]; 5-OAc, 0.71.[19] The ΔG value was calculated to be 5.07 kJ/mol, corresponding to the equilibrium proportion of 2e/5a-conformer:2a/5e-conformer = 89:11 at 298 K. This means that the repeating unit of polyester **4** predominantly takes the conformation having the carbonyl carbon atom in the equatorial position and the ester oxygen atom in the axial position of the tetrahydropyran ring.



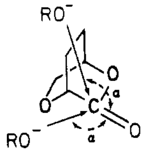
cis-9, 2e/5a cis-9, 2a/5e (3)

$$\Delta G = 5.07 \text{ kJ/mol}$$
$$K = \frac{[2a/5e]}{[2e/5a]} = \frac{11}{89} \quad (\text{at } 298 \text{ K})$$

The formation of the polyester exclusively composed of the cis-disubstituted tetrahydropyran unit definitely proves that the acyl-oxygen scission of the ester linkage occurs when **3** is polymerized with anionic initiators. This is another way of saying that the propagating species is an alkoxide anion and that side reactions altering the configurations of the asymmetric carbons in the repeating units, such as proton abstraction from the methine group adjacent to the carbonyl group, are negligible under the reaction conditions employed.

In relation to the mechanism of the anionic polymerization of **3**, the polymerization behavior of 2-oxabicyclo[2.2.2]octan-3-one reported by Ceccarelli et al.[20] is worthy of note: According to their interpretation, the polymerization initiated with *n*-butyllithium propagates by alkoxide growing species, whereas the polymerization initiated by sodium *tert*-butoxide and sodium–potassium alloy propagates by both alkoxide and carboxylate growing species to give polyester comprised of cis- and trans-1,4-linked cyclohexane rings.

Reactivity. As inferred from the data in Table I, the reactivity of **3** in its anionic and coordination polymerization is unexpectedly low. One of the reasons is, as described earlier, that because of the poor solubility of the polymer, the growing species are occluded in the precipitated polymer as the polymerization proceeds. Besides this, the low reactivity is attributable, at least in part, to steric hindrance encountered when an alkoxide growing anion approaches a monomer molecule and also to synperiplanar interactions of the polar carbon–oxygen bonds with the electron pairs on the adjacent oxygen atom in the adduct of the growing anion with the carbonyl carbon atom of the monomer.[21] According to the quantum chemical calculation by Burgi et al.,[22] a nucleophile approaches a carbonyl carbon atom along the path for which the angle α between the line joining the nucleophile with the carbonyl carbon and the direction of the C=O bond is in general 100–110°. If this is the case in the anionic polymerization of 3, a considerable steric hindrance must be overcome, from whichever sides of the plane containing the ester linkage an alkoxide anion attacks the carbonyl carbon atom (**10**). Furthermore, the addition of an alkoxide anion to the carbonyl carbon converts the sp^2 carbon atom to the sp^3 carbon, thus giving rise to synperiplanar interactions of the polar C–O$^-$ and C–OR bonds with the electron pairs of the adjacent O(2) atom (**11**).[23] In addition, a synperiplanar interaction arises also between one of the polar C–O bonds and the electron pair of the O(5) atom. This is also responsible for making the formation of the adduct 11 energetically unfavorable. The relatively low reactivity of 1 in its anionic polymerization reported in the previous paper[1] also can be reasonably accounted for by taking these factors into consideration.



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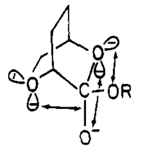

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In the present case, propagation by a carboxylate growing anion can be excluded, because the polyester obtained was entirely composed of cis-2,5-linked tetrahydropyran rings. Therefore, it seems likely that the strain energy of the bicyclic lactone 3 is not so large as to allow the formation of a carboxylate anion by the attack of a growing anion on the bridgehead C(1) atom of the monomer. In fact, the strain energy of 2-oxabicyclo[2.2.2]octan-3-one, an analogue of 1 and 3, has been reported to be 41.5 kJ/mol on the basis of the measurement of the enthalpies of combustion for the monomer and its polymer.[24] This value is much smaller than the strain energies of β-propiolactone (94.2 kJ/mol)[25] and pivalolactone (85.8 kJ/mol),[26] which can undergo anionic polymerization through the alkyl-oxygen scission as well as the acyl-oxygen scission of the lactone ring.

The poor cationic polymerizability of 3 may be interpreted as follows. Addition of cationic species is most likely to take place on the carbonyl oxygen atom having the highest electron density in the monomer.[27,28] In this case, ring-opening reaction occurs only through the alkyl-oxygen scission of the ester linkage. However, such bond cleavage seems to take place very reluctantly, because of the relatively small strain energy of the bicyclic structure. In fact, the polyester obtained with trifluoromethanesulfonic acid exclusively consisted of cis-2,5-linked tetrahydropyran rings, implying that polymerization proceeded through the acyl-oxygen scission, and not through the alkyl-oxygen scission, of the lactone ring. This is in sharp contrast to the behavior of 1, in which the alkyl-oxygen scission is facilitated by the presence of the adjacent endocyclic oxygen atom. If cationic species add onto the ester oxygen atom O(2) of 3, the resulting oxonium ion would be cleaved at the acyl-oxygen bond by the nucleophilic addition of the monomer on the electropositive carbonyl carbon atom. Such nucleophilic addition of the bulky monomer, however, should be hindered for the aforementioned reasons, thus lowering the cationic polymerizability of 3.

Experimental Section

Preparation of Ethyl 3,4-Dihydro-2*H*-pyran-2-carboxylate (6). A mixture of sodium 3,4-dihydro-2*H*-pyran-2-carboxylate (150.0 g, 1.0 mol), ethyl iodide (192.3 g, 1.2 mol), sodium carbonate (10 g), and dimethylformamide (500 mL) was heated at 105–110 °C for 5 h. The reaction mixture was cooled to room temperature, and water (450 mL) was added to dissolve inorganic salts. The mixture was extracted with four 200-mL portions of benzene. The combined organic layers were washed with four 200-mL portions of water and dried over anhydrous magnesium sulfate. The solution was filtered and the solvent was removed by rotary evaporation. The oily residue was distilled under reduced pressure: yield 135.2 g (87%); bp 75–80 °C (8 mmHg); IR (neat) 3060 ($\nu_{=C-H}$), 1760 ($\nu_{C=O}$), 1650 ($\nu_{C=C}$), 1200 (ν_{C-O-C}), 1080 (ν_{C-O-C}) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 6.42 (d, J = 6.2 Hz, 1 H, H-6), 4.76 (m, 1 H, H-5), 4.45 (m, 1 H, H-2), 4.24 (q, J = 7.2 Hz, 2 H, CH_2CH$_3$), 1.9–2.2 (m, 4 H, 2H-3 and 2H-4), 1.30 (t, J = 7.2 Hz, 3 H, CH$_2$CH_3); ^{13}C NMR (CDCl$_3$) δ 170.96 (C=O), 142.63 (C-6), 100.70 (C-5), 73.12 (C-2), 61.06 (CH$_2$CH$_3$), 24.88 (C-3), 18.52 (C-4), 14.18 (CH$_2$$CH_3$).

Preparation of Ethyl 5-Hydroxytetrahydropyran-2-carboxylate (7). Ethyl 3,4-dihydro-2*H*-pyran-2-carboxylate (40.0 g, 0.26 mol) and dry tetrahydropyran (350 mL) were charged into a 1-L three-necked flask equipped with a dropping funnel. The solution was cooled with a dry ice–acetone bath to −5 °C, and a freshly prepared borane solution in tetrahydrofuran (100 mL, 0.12 mol)[2] was added through the dropping funnel over a period of 2 h. The solution was stirred at 0 °C overnight.

(i) Oxidation with Sodium Dichromate–Sulfuric Acid. Water was carefully added to the solution to destroy excess borane. The reaction mixture was cooled in a dry ice–acetone bath and an oxidizing reagent prepared by dissolving sodium dichromate dihydrate (56.8 g, 0.20 mol) in a mixture of concentrated sulfuric acid (42 mL) and water (230 mL) was added slowly, keeping the solution temperature at 3–7 °C. After the addition of the oxidizing reagent, the solution was stirred at 3–7 °C for 1 h. Sodium bisulfite (83.0 g) was added in portions until the brown color of the upper layer almost disappeared. The upper layer was separated and the green viscous lower layer was extracted with four 50-mL portions of ethyl ether. The combined organic layers were washed with four 50-mL portions of a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate. The drying agent was filtered and the solvent was removed by a rotary evaporator to give viscous oil. It was a mixture of the cis and trans isomers (1:~1 by ^{13}C NMR); yield 32.4 g (72%).

(ii) Oxidation with Alkaline Hydrogen Peroxide. The reaction mixture was cooled to −10 °C and a solution of sodium acetate trihydrate (30.4 g, 0.23 mol) in water (45 mL) was cautiously added. Foams were violently evolved for the first several drops. After the addition was completed, 30% aqueous hydrogen peroxide (30 mL, 0.26 mol) was slowly added to the reaction mixture, keeping the temperature at 30 ± 5 °C. The reaction mixture was then stirred at room temperature for 1.5 h. The reaction mixture was salted out, and the resulting organic layer was separated from the aqeuous layer. The aqueous layer was extracted with three 70-mL portions of tetrahydrofuran. The combined organic layers were dried over anhydrous magnesium sulfate. After filtration, rotary evaporation of the solvent from the filtrate gave a viscous light yellow oil containing a small amount of white powder. Anhydrous ether (100 mL) was added to dissolve the oil, and the white powder was removed by filtration. Evaporation of the solvent and subsequent distillation under reduced pressure gave a slightly yellow viscous oil. It was a mixture of the cis and trans isomers (1:9 by ^{13}C NMR): yield 28.4 g (71%); bp 98–107 °C (0.4 mmHg); IR (neat) 3400 (ν_{O-H}), 1740 ($\nu_{C=O}$), 1210 (ν_{C-O-C}), 1090 (ν_{C-O-C}) cm^{-1}; ^{1}H NMR (CDCl$_3$) cis isomer, δ 4.24 (q, J = 7.2 Hz, 2 H, CH_2CH$_3$), 4.05 (dd, J = 2.6 Hz, J = 10.6 Hz, 1 H, H-6), 3.97 (dd, J = 2.5 Hz, J = 11.7 Hz, 1 H, H-2), 3.82–3.68 (m, 1 H, H-5), 3.65 (dd, J = 2.2 Hz, J = 10.6 Hz, 1 H, H-6), 2.50 (br, 1 H, OH), 2.15–1.75 (m, 4 H, 2H-3 and 2H-4), 1.29 (t, J = 7.2 Hz, 2H-3 CH$_2$CH_3); ^{1}H NMR trans isomer, δ 4.23 (q, J = 7.2 Hz, 2 H, CH_2CH$_3$), 4.12 (dd, J = 4.5 Hz, J = 11.0 Hz, 1 H, H-6), 3.95 (dd, J = 2.4 Hz, J = 10.4 Hz, 1 H, H-2), 3.85–3.70

(m, 1 H, H-5), 3.21 (dd, J = 9.6 Hz, J = 11.0 Hz, 1 H, H-6), 2.50 (br, 1 H, OH), 2.25–1.40 (m, 4 H, 2H-3 and 2H-4), 1.29 (t, J = 7.2 Hz, 3 H, CH_2CH_3); ^{13}C NMR ($CDCl_3$) cis isomer, δ 171.48 (C=O), 75.73 (C-2), 71.88 (C-6), 63.98 (C-5), 61.21 (CH_2CH_3), 29.43 (C-3), 23.62 (C-4), 14.18 (CH_2CH_3); ^{13}C NMR trans isomer, δ 171.14 (C=O), 75.43 (C-2), 72.02 (C-6), 64.96 (C-5), 61.21 (CH_2CH_3), 31.67 (C-3), 27.24 (C-4), 14.18 (CH_2CH_3).

Preparation of 2,5-Dioxabicyclo[2.2.2]octan-3-one (3). A mixture of the cis and trans isomers of ethyl 5-hydroxytetrahydropyran-2-carboxylate (3.9 g, 0.023 mol) was dissolved in dry toluene (200 mL). *p*-Toluenesulfonic acid monohydrate (0.20 g, 1.1 mmol) was added as a catalyst. The mixture was refluxed for 7 h through a Soxhlet extractor containing molecular sieves 5A in a thimble. The mixture was cooled to room temperature, and anhydrous sodium carbonate (5 g) was added to neutralize the acid. The solution was passed through a short pad of silica gel and concentrated. A brown viscous oil was subjected to column chromatography (column, silica gel; eluent, 1:1 (v/v) *n*-hexane/ethyl acetate). The crude product thus isolated was purified by repeated recrystallization from a mixture of ethyl ether and *n*-hexane ((5-10):1 (v/v)): yield 0.95 g (33%); mp 56–57 °C; IR (KBr) 1760 ($\nu_{C=O}$), 1230 (ν_{C-O-C}) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.77 (m, 1 H, H-1), 4.26 (dd, 1 H, H-4), 4.04–3.94 (m, 2 H, 2H-6), 2.40–1.85 (m, 4 H, 2H-7 and 2H-8); ^{13}C NMR ($CDCl_3$) δ 170.85 (C=O), 73.28 (C-4), 67.61 (C-1), 66.02 (C-6), 24.00 (C-8), 22.87 (C-7); mass spectrum, m/e 128, 84, 69, 55, 43, 41, 29. Anal. Calcd for $C_6H_8O_3$: C, 56.30; H, 6.30. Found: C, 56.24; H, 6.29. Monoclinic space group $P2_1/c$; a = 5.686 (1) Å, b = 7.076 (1) Å, c = 14.910 (3) Å, β = 97.02 (2)°; ρ = 1.43 g/cm^3.

Preparation of Methyl 5-Acetoxytetrahydropyran-2-carboxylate (9). (i) Cis Isomer. Sodium methoxide (0.01 g, 0.2 mmol) was added to a solution of **3** (0.30 g, 2.3 mmol) dissolved in methanol (10 mL). The mixture was stirred at room temperature for 2 h. After neutralization with acetic acid, the solvent was removed on a rotary evaporator under reduced pressure to give *cis*-methyl 5-hydroxytetrahydropyran-2-carboxylate as colorless oil: ^1H NMR ($CDCl_3$) δ 5.53 (br s, 1 H, OH), 4.05 (dd, J = 2.6 Hz, J = 10.4 Hz, 1 H, H-2), 3.97 (br d, J = 11 Hz, 1 H, H-6_{eq}), 3.8–3.7 (m, 1 H, H-5), 3.76 (s, 3 H, OCH_3), 3.62 (dd, J = 2.2 Hz, J = 10.8 Hz, H-1, H-6_{ax}), 2.1–1.8 (m, 4 H, 2H-3 and 2H-4); ^{13}C NMR ($CDCl_3$) δ 171.64 (C=O), 75.41 (C-2), 71.76 (C-6), 63.80 (C-5), 52.07 (OCH_3), 29.37 (C-3), 23.60 (C-4).

The hydroxytetrahydropyran derivative was dissolved in acetic anhydride (2 mL) and pyridine (3 mL), and the mixture was stirred at room temperature for 2 H. It was diluted with dichloromethane (30 mL). The solution was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate. The mixture was filtered and the filtrate was freed from the solvent on a rotary evaporator under reduced pressure to give *cis*-methyl 5-acetoxytetrahydropyran-2-carboxylate as a colorless oil: ^1H NMR ($CDCl_3$) δ 4.80 (br s, 1 H, H-5), 4.2–4.0 (m, 2 H, H-2 and H-6_{eq}), 3.76 (s, 3 H, OCH_3), 3.69 (dd, J = 2.1 Hz, J = 12.3 Hz, H-6_{ax}), 2.08 (s, 3 H, CH_3CO), 2.05–1.85 (m, 4 H, 2H-3 and 2H-4); ^{13}C NMR ($CDCl_3$) δ 170.86 ($COOCH_3$), 170.06 (CH_3CO), 75.26 (C-2), 68.95 (C-6), 66.56 (C-5), 51.95 (OCH_3), 26.90 (C-3), 24.03 (C-4), 21.07 (CH_3CO).

(ii) Trans Isomer. Ethyl 5-hydroxytetrahydropyran-2-carboxylate (1.5 g, 8.6 mmol) rich in trans isomer prepared by hydroboration of **6** followed by oxidation with alkaline hydrogen peroxide was dissolved in methanol (50 mL) containing a drop of concentrated sulfuric acid and the solution was stirred at room temperature overnight. After neutralization with sodium hydroxide, the mixture was freed from the solvent on a rotary evaporator to afford methyl 5-hydroxytetrahydropyran-2-carboxylate as a colorless viscous oil: ^1H NMR ($CDCl_3$) δ 4.14–4.06 (m, 1 H, H-6_{eq}), 3.96 (dd, J = 2.1 Hz, J = 11 Hz, 1 H, H-2), 3.77 (s, 3 H, OCH_3), 3.75–3.69 (m, 1 H, H-5), 3.31 (br s, 1 H, OH), 3.20 (dd, J = 10 Hz, J = 11 Hz, 1 H, H-6_{ax}), 2.2–1.4 (m, 4 H, 2H-3 and 2H-4); ^{13}C NMR ($CDCl_3$) δ 171.30, (C=O), 75.31 (C-2), 71.98 (C-6), 64.89 (C-5), 52.10 (OCH_3), 31.61 (C-3), 27.76 (C-4).

The hydroxytetrahydropyran derivative was acetylated in a manner similar to the procedure described for the cis isomer to yield methyl 5-acetoxytetrahydropyran-2-carboxylate rich in trans isomer as a colorless liquid: ^1H NMR ($CDCl_3$) δ 4.8–4.7 (m, 1 H, H-5), 4.18–4.13 (m, 1 H, H-6_{eq}), 4.06 (dd, J = 1.9 Hz, J = 8.8 Hz, 1 H, H-2), 3.77 (s, 3 H, OCH_3), 3.37 (dd, J = 8.8 Hz, J = 11.2 Hz, 1 H, H-6_{ax}), 2.2–1.6 (m, 4 H, 2H-3 and 2H-4), 2.05 (s, 3 H, CH_3CO); ^{13}C NMR ($CDCl_3$) δ 170.84 ($COOCH_3$), 170.23 (CH_3CO), 74.99 (C-2), 68.29 (C-6), 67.03 (C-5), 27.75 (C-3), 26.35 (C-4).

Polymerization Procedures. Antimony pentachloride, boron trifluoride etherate, trifluoromethanesulfonic acid, and tetraisopropyl titanate were distilled just before use. Phosphorus pentafluoride was generated by heating *p*-chlorobenzenediazonium hexafluorophosphate. Lithium benzophenone ketyl was prepared from benzophenone and lithium metal in tetrahydrofuran. *n*-Butyllithium was used as supplied. Polymerization was carried out, in most cases, in a high-vacuum system. After a specified time, pyridine (for cationic polymerization) or acetic acid (for anionic polymerization) was added to terminate the polymerization. The mixture was then poured into a large volume of methanol to precipitate a polymer. The polymer was purified by repeated reprecipitation from dichloromethane solution with methanol: IR (KBr) 1745 ($\nu_{C=O}$), 1205 (ν_{C-O-C}), 1120 (ν_{C-O-C}) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.93 (1 H, H-5), 4.2–4.0 (2 H, H-2 and H-6_{eq}), 3.68 (1 H, H-6_{ax}), 2.2–1.7 (4 H, 2H-3 and 2H-4); ^{13}C NMR data are given in Table III. Anal. Calcd for $(C_6H_8O_3)_n$: C, 56.24; H, 6.29. Found: C, 56.54; H, 6.63.

Characterization. ^1H and ^{13}C NMR spectra were recorded on a JEOL FX-200 instrument operating at 200 (^1H) and 50 MHz (^{13}C), respectively. Deuteriochloroform and tetramethylsilane were used as the solvent and internal reference. Infrared spectra were measured with a Jasco A-3 spectrophotometer. Molecular weights of the polymers were estimated by using a Hitachi 634A gel permeation chromatograph (column, Shodex A80M, 1 m; eluent, chloroform; polystyrene standard). Thermal properties of the polymer were determined by a Perkin-Elmer differential scanning calorimeter Model DSC-2.

Acid-Catalyzed Solvolysis. The rates of acid-catalyzed solvolysis of bicyclic lactones were determined at 25 °C in a mixture of acetone-d_6 and deuterium oxide (4:1 (v/v)) in the presence of dichloroacetic acid as catalyst. The initial concentrations of the lactones and of the catalyst were 1.0 and 0.05 mol/L, respectively. The reaction was followed by monitoring the changes of the acetal proton signals (**1** and **8**) or of the C-4 methine proton signals (**3**).

Acknowledgment. This research is one of a series of works of the U.S.–Japan Cooperative Science Program supported by the National Science Foundation, Division of Materials Research, and the Japan Society for the Promotion of Science.

Registry No. **3**, 100514-01-0; **3** (homopolymer), 100762-90-1; **3** (SRU), 63413-82-1; **5**, 16698-52-5; **6**, 83568-11-0; *cis*-**7**, 100514-02-1; *trans*-**7**, 100514-05-4; *trans*-**9**, 100514-03-2; *cis*-**9**, 100514-04-3; benzophenone monolithium complex, 16592-10-2; ethyl iodide, 75-03-6; trifluoromethanesulfonic acid, 1493-13-6; butyllithium, 109-72-8; tetraisopropyl titanate, 546-68-9; sodium methoxide, 124-41-4.

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Kinetics and Mechanism of the Boron Trichloride Catalyzed Thermal Ring-Opening Polymerization of Hexachlorocyclotriphosphazene in 1,2,4-Trichlorobenzene Solution

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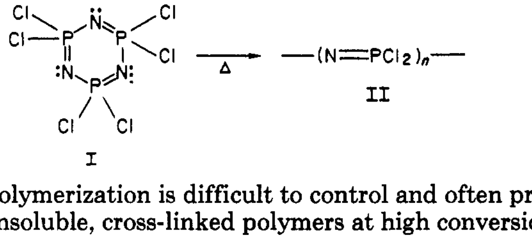
Received September 23, 1985

ABSTRACT: The products and kinetics of the boron trichloride (BCl_3) catalyzed thermal ring-opening polymerization of hexachlorocyclotriphosphazene ($(NPCl_2)_3$) have been investigated in 1,2,4-trichlorobenzene solution at 170–230 °C in sealed glass tubes under vacuum. Polymeric products were characterized by high-performance size exclusion chromatography, membrane osmometry, light scattering, and dilute solution viscometry. The BCl_3-catalyzed polymerization is not cocatalyzed by water, but polymerization is strongly inhibited by aryl phosphates. Polymerization rates were determined by monitoring $(NPCl_2)_3$ concentration with laser Raman spectroscopy. The kinetic data fit a mechanism that involves initiation, catalysis, and inhibition of polymerization by BCl_3, depending on the experimental conditions.

Introduction

The thermal ring-opening polymerization of hexachlorocyclotriphosphazene ($(NPCl_2)_3$ (I)) (eq 1) is the principal synthetic route to poly(dichlorophosphazene) (II), which is the precursor to the technologically promising poly(organophosphazenes). Unfortunately, the uncatalyzed polymerization is difficult to control and often produces insoluble, cross-linked polymers at high conversion which are almost useless for preparing the organosubstituted polymers.[1] Variations in chloro polymer characteristics are even observed between different batches of I under the same polymerization conditions. The thermal polymerization has been studied extensively and is reviewed in recent literature.[2] It is generally agreed that the reaction is a cationic chain growth polymerization. The initiation mechanism is frequently proposed to be one of two processes, either ring opening of I or Cl⁻ dissociation from I (eq 2 and 3).[3-5]



(1)

I

$$\mathrm{I} \rightarrow {}^{-}\mathrm{N{=}(PCl_2N)_2{=}PCl_2^{+}} \quad (2)$$

$$\mathrm{I} \rightleftharpoons (\mathrm{N_3P_3Cl_5})^{+}\,\mathrm{Cl^{-}} \quad (3)$$

A great many compounds have been found to promote the polymerization of I.[2,6,7] Although many catalysts increase the polymerization rate and are effective at promoting polymerization of I at temperatures lower than those required for the uncatalyzed reaction, the majority also enhance the tendency of the reaction to form cross-linked material. Boron trichloride (BCl_3) is an effective catalyst for the reaction, promoting polymerization at temperatures as low as 150 °C to give >80% soluble polymeric II.[8] There have been few kinetic studies of the catalyzed polymerization and none reported for BCl_3.

We have studied the BCl_3-catalyzed thermal solution polymerization of I and propose a mechanism which should