Spontaneous Hydrolytic Degradability of Copolyesters Having Tetrahydropyran Rings in Their Backbones

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SYNOPSIS

Homo- and copolyesters, containing 2,5-linked tetrahydropyran rings in their backbones, were prepared by cationic ring-opening polymerization of bicyclic lactones, 2,6-dioxabicyclo[2.2.2]octan-3-one (1), and its 4-methoxy-carbonyl and 4-benzyloxycarbonyl derivatives (3 and 4). Copolyesters, having pendant carboxyl groups, were derived from the copolymers containing 4 as one of the comonomers by the catalytic hydrogenolysis of the pendant benzyloxy–carbonyl groups. Copolyesters, containing both 2,5-linked and 2,6-linked tetrahydropyran rings in the main chains, were obtained by the copolymerization of 1 with 6,8-dioxabicyclo[3.2.1]octan-7-one (13), which is a structural isomer of 1. Spontaneous hydrolytic degradability of these polyesters was investigated in a phosphate buffer solution (pH 7.5) at 27°C. The degradability of the polyesters markedly depended on the molecular structure: hydrophobic pendant groups retarded the hydrolytic degradation, whereas hydrophilic pendant groups accelerated it. In particular, a small amount of pendant carboxyl groups significantly enhanced the hydrolytic degradability of the copolyesters from 1. Polyesters, containing 2,6-linked tetrahydropyran rings in their backbones, underwent hydrolytic degradation more readily than those entirely consisting of 2,5-linked tetrahydropyran rings. © 1994 John Wiley & Sons, Inc.

INTRODUCTION

Pollution by wasted plastics is one of the major factors that are worsening the ecological environment on the earth. There are two approaches to solving this troublesome problem: one is the material design of readily recyclable polymers; the other is the development of spontaneously degradable polymeric materials. As for the latter approach, one of the most promising materials is a class of photodegradable polymers. A variety of photodegradable polymers have been designed and synthesized, and some of them are commercialized.[1] Polymers, which are spontaneously hydrolyzable under neutral conditions to yield harmless low molecular weight compounds, would be of practical value if they were readily processable and had the desirable mechanical and thermal properties. Of particular importance are biodegradable polymers, which are hydrolyzed and catabolized by microorganisms in a natural environment.

On the other hand, from the viewpoint of biomedical materials, considerable attention has been directed toward spontaneously hydrolyzable, biodegradable, synthetic polymers, especially poly(α-hydroxy acid)s, such as poly(glycolic acid), poly(lactic acid), and their analogues.[2] Since the hydrolysis rates of these polyesters are relatively low, because of their high crystallinity and low hydrophilicity, several biodegradable polyesters with pendant carboxyl groups have been synthesized in order to impart higher hydrophilicity. Lenz et al.[3,4] prepared homo- and copolymers of β-malic acid and its alkyl esters by ring-opening polymerization of benzyl malolactonate, followed by hydrogenolytic debenzylation. Ouchi and Fujino[5] prepared poly(α-malic acid) from malide dibenzyl ester and examined its hydrolysis in vitro. Kimura et al.[6] prepared an al-

ternating copolymer of α-malic acid and glycolic acid in a similar manner. Subsequently, in't Veld et al.[7] obtained polyesteramide with pendant carboxylic groups from morpholine derivatives.

In our laboratory, efforts have been devoted to the synthesis of a series of new specialty polymers, having tetrahydropyran or tetrahydrofuran rings in their backbones, chiefly by ring-opening polymerization of bicyclic acetals, lactones, and lactams.[8,9] During the course of the investigations, polyester **2** [IUPAC nomenclature, poly(tetrahydropyran-5,2-diyloxycarbonyl)], readily obtainable from 2,6-dioxabicyclo[2.2.2]octan-3-one (**1**), was found to undergo spontaneous hydrolysis in a neutral buffer solution at ambient temperature, eventually producing 6-hydroxytetrahydropyran-2-carboxylic acid.[10,11] A film of polyester **2** was also disintegrated after it had been buried in soil for a few months. These findings prompted us to undertake further investigation on the spontaneous hydrolytic degradability, as well as on biodegradability of the polyester and its homologues.

1   **2**
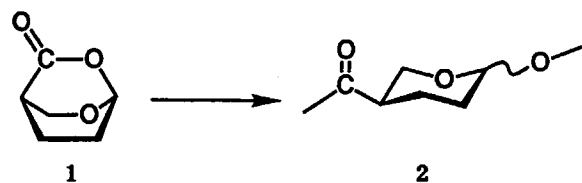
This article is concerned with structural factors affecting the spontaneous hydrolytic degradability of polyesters and copolyesters containing tetrahydropyran rings in their backbones. Potential biodegradability of these polyesters will be described in a subsequent article.[12]

EXPERIMENTAL

General Methods

^{1}H- and ^{13}C-NMR spectra were recorded on a JEOL JNM EX-270 spectrometer, operating at 270 MHz (^{1}H) and 67.5 MHz (^{13}C), respectively. Deuteriochloroform and tetramethylsilane were used as solvent and internal reference. Molecular weights of the polymers were estimated by gel permeation chromatography (column, TSK-gel G2000HXL and G3000HXL; eluent, chloroform; polystyrene standard).

Monomers.

2,6-Dioxabicyclo[2.2.2]octan-3-one (**1**) and its 4-methoxycarbonyl and 4-benzyloxycarbonyl derivatives (**3** and **4**) were synthesized from acrolein and dimethyl malonate, according to the procedures previously reported.[13,14] 6,8-Dioxabicyclo[3.2.1]octan-7-one (**13**) was prepared from sodium 3,4-dihydro-2H-pyran-2-carboxylate.[15] These monomers were purified as described in the previous articles.[13,14]

Polymerization.

Cationic homo- and copolymerizations of the bicyclic lactones were carried out in dichloromethane at temperatures at or below −60°C, with boron trifluoride etherate as an initiator. A high vacuum technique was employed for the polymerization. After the polymerization was terminated, by the addition of a small amount of pyridine, the reaction mixture was poured into a large volume of methanol to precipitate a polymer. It was purified by repeated reprecipitation, using dichloromethane and methanol as a solvent-precipitant pair, and was dried under reduced pressure to a constant weight.

Hydrolysis of Polyesters

A sample of polyester (25 mg) was taken in each of several test tubes. A small amount of chloroform was added to dissolve the sample. By rotating the test tube and slowly evaporating the solvent, the bottom part (about 2 cm) of the inner wall of the test tube, was coated with a thin film of the polyester. A phosphate buffer solution (5 mL, pH 7.5) was added to each test tube. The test tubes were allowed to stand in a room, thermostated at 27°C. At specified intervals, the aqueous solution of one of the test tubes was separated from the insoluble polymer by decantation. The water insoluble polymer was washed with water, was dried under vacuum, and was weighed. The number average molecular weight of the water-insoluble polymer was determined by gel permeation chromatography.

Water was evaporated from the separated aqueous solution and the resulting residue was extracted with acetone. The acetone extract was analyzed by ^{1}H-NMR spectroscopy.

Hydrolysis of Model Compounds

Methyl 6-acetoxytetrahydropyran-2-carboxylate or methyl 6-acetoxytetrahydropyran-3-carboxylate (10 mg) was weighed in an NMR tube. A mixed solvent of methanol-d_4 and deuterium oxide (7 : 1, v/v) was added into the tube to dissolve the sample. The hydrolysis was followed by monitoring the ^{1}H–NMR spectrum. The conversion of the substrates to the corresponding hydroxytetrahydropyran carboxylic acids was determined from the relative peak intensity of the acetoxy methyl protons of the substrate and the methyl protons of the liberated acetic acid.

RESULTS AND DISCUSSION

Spontaneous Hydrolysis Behavior of Copolyesters Having Pendant Alkoxycarbonyl Groups

Two series of copolyesters, having pendant benzyloxycarbonyl groups, were prepared by cationic ring-opening copolymerization of 2,6-dioxabicyclo[2.2.2]octan-3-one (1) or its 4-methoxycarbonyl derivative (3) with the 4-benzyloxycarbonyl derivative (4). The copolymer composition was determined from the relative peak areas of the phenyl and anomeric protons in the ^{1}H–NMR spectrum. The results are summarized in Tables I and II.

1, R=H   4   5, R=H
3, R=CO$_2$ CH$_3$ 6, R=CO$_2$ CH$_3$
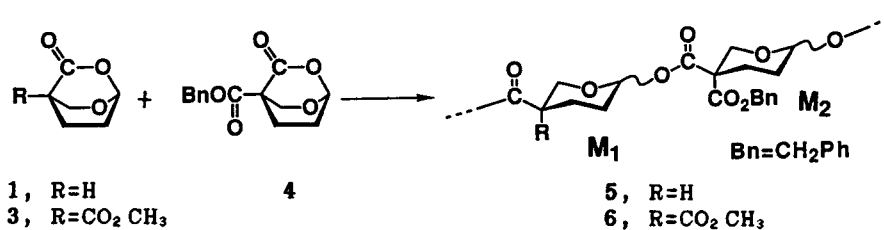
The copolymerization of 1 with 4 proceeded rapidly. Moreover, the reactivity of 1 is higher than that of 4 and, hence, it was difficult to synthesize copolymers with controlled composition and distribution of the comonomer units. In contrast, judging from the copolymer composition and the comonomer composition in feed, the reactivities of 3 and 4 in

their copolymerization are similar, and the content of the pendant benzyloxycarbonyl groups in the resulting copolyesters can be easily controlled. These polyesters were capable of forming films by casting.

Spontaneous hydrolysis of these polyesters were investigated by monitoring the changes in the weight and molecular weight of films during immersion in

Table I   Copolymerizaton of 2,6-dioxabicyclo[2.2.2]octan-3-one (1) with 4-benzyloxycarbonyl-2,6-dioxabicyclo[2.2.2]octan-3-one (4)

Mol Frac. of 4 in Feed	[M]$_0$^{a} (mol/L)	Init.^{b} (mol %)	Temp. (°C)	Time (min)	Yield (%)	Mol Frac. of 4 in Copolymer^c	M$_n$^{d} × 10^{-4}	$\dfrac{M_w{}^d}{M_n}$
1.00	1.0	5	−60	17 h	95	1.00	4.9	1.3
0.40	1.0	2	−60	10	93	0.37	1.4	2.3
0.33	1.0	3	−60	1	68	0.12	2.7	1.5
0.30	0.5	1	−78	7	60	0.03	3.0	1.6
0.20	0.5	1	−78	1	38	0.01	2.7	1.4
0.09	0.5	2	−60	1	85	0.02	4.8	1.3
0.09	0.5	1	−78	10	16	0.01	2.0	2.1
0.00	1.0	2	−60	20	94	0.00	3.5	1.5

^{a} Initial total monomer concentration; solvent, CH$_2$Cl$_2$.
^{b} Initiator, BF$_3$OEt$_2$.
^{c} Determined by ^{1}H–NMR.
^{d} Determined by GPC (polystyrene standard).

Table II   Copolymerizaton of 4-methoxycarbonyl-2,6-dioxabicyclo[2.2.2]octan-3-one (3) with 4-benzyloxycarbonyl-2,6-dioxabicyclo[2.2.2]octan-3-one (4)

Mol Frac. of 4 in Feed	$[M]_0$[a] (mol/L)	Init.[b] (mol %)	Temp. (°C)	Time (h)	Yield (%)	Mol Frac. of 4 in Copolymer[c]	M_n[d] $\times$ 10^{-4}	$\dfrac{M_w{}^d}{M_n}$
1.00	0.5	5	−60	17	95	1.00	4.9	1.3
0.50	0.5	1	−78	2	28	0.45	3.1	1.3
0.05	0.5	1	−78	11	22	0.08	2.5	1.6
0.03	1.0	1	−60	3	73	0.04	3.7	1.3
0.02	0.5	1	−78	8	39	0.02	1.9	1.6
0.00	1.0	2	−60	1.5	67	0.00	4.1	1.4

[a] Initial total monomer concentration; solvent, CH_2Cl_2.
[b] Initiator, BF_3Et_2O.
[c] Determined by ^1H-NMR.
[d] Determined by GPC (polystyrene standard).

a phosphate buffer solution (pH 7.5) at 27°C. Figure 1 shows typical results on the films of three homo-polyesters **2**, **7**, and **8**.
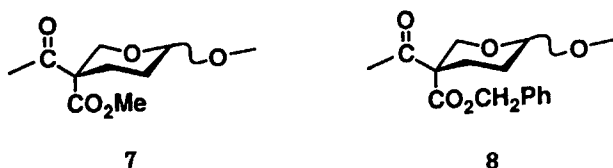
As is clearly seen in Figure 1, unsubstituted polyester **2** showed the fastest decrease in molecular weight, whereas polyester **8**, bearing hydrophobic benzyloxycarbonyl pendant groups, showed the slowest decrease. Polyester **7**, having methoxycar-

bonyl groups, exhibited slightly lower hydrolyzability than polyester **2**, as far as the molecular weight decrease is concerned. There were only slight differences in the recovery of polymer among the three polyesters up to the immersion for 21 days, but the recovery for polyester **2** dropped to 64% after immersion for 28 days. Apparently, the lower molecular weight polymers, produced from polyester **2**, were lost because of their solubility in the medium.

Water soluble products were separated and analyzed by ^1H-NMR spectroscopy. They were mostly the corresponding hydroxytetrahydropyran carboxylic acids. This means that oligoesters, dissolved in the medium, are hydrolyzed much faster than the original polyesters in their film state.

Figures 2 and 3 demonstrate the decrease of the molecular weight for the two series of copolyesters
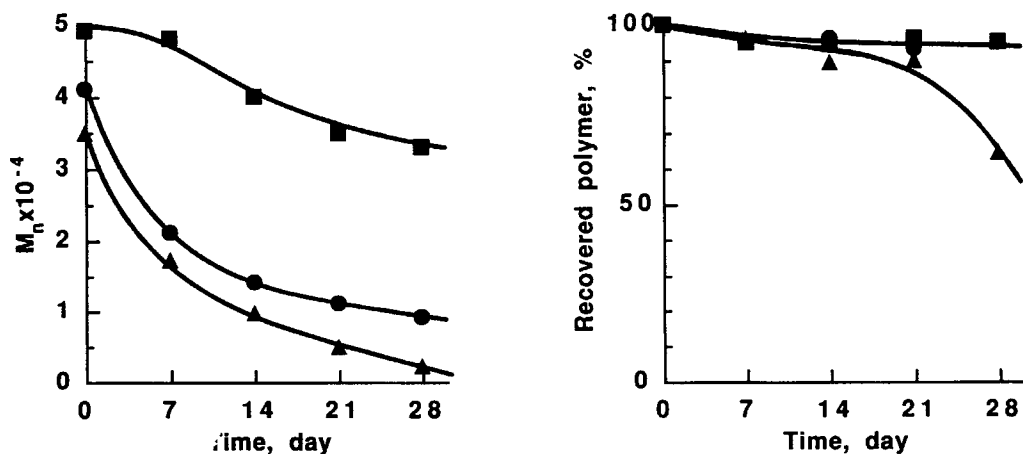

Figure 1   Changes in the molecular weight (left) and recovery of polymer (right) during the heterogeneous hydrolysis of homopolyesters **2**, **7**, and **8**. Phosphate buffer, pH 7.5; temp., 27°C. (▲) polyester **2**, (●) polyester **7**, and (■) polyester **8**.
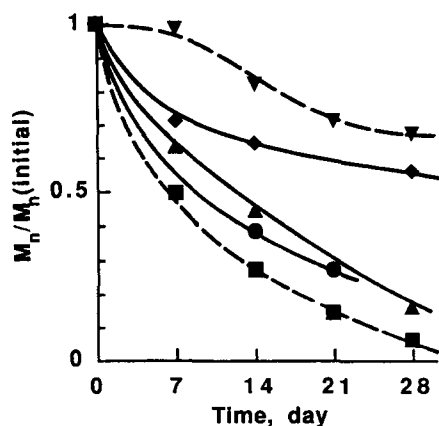
Figure 2 Molecular weight changes during the heterogeneous hydrolysis of copolyester **5** composed of unsubstituted (M_1) and benzyloxycarbonyl-substituted (M_2) tetrahydropyran rings. Phosphate buffer, pH 7.5; temp., 27°C. (▼) $M_1 : M_2 = 0 : 100$ ($M_n = 4.9 \times 10^4$), (♦) $M_1 : M_2 = 63 : 37$ ($M_n = 1.4 \times 10^4$), (▲) $M_1 : M_2 = 88 : 12$ ($M_n = 2.7 \times 10^4$), (●) $M_1 : M_2 = 99 : 1$ ($M_n = 2.0 \times 10^4$), and (■) $M_1 : M_2 = 100 : 0$ ($M_n = 3.5 \times 10^4$).
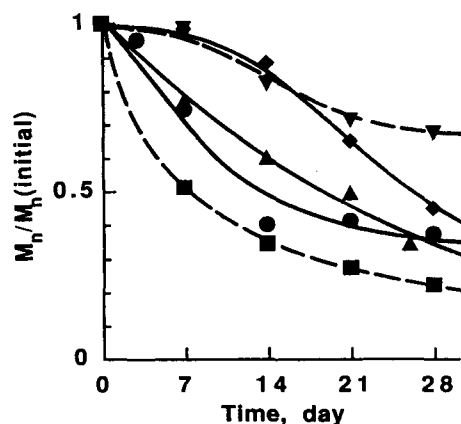
Figure 3 Molecular weight changes during the heterogeneous hydrolysis of copolyester **6** composed of methoxycarbonyl-substituted (M_1) and benzyloxycarbonyl-substituted (M_2) tetrahydropyran rings. Phosphate buffer, pH 7.5; temp., 27°C. (▼) $M_1 : M_2 = 0 : 100$ ($M_n = 4.9 \times 10^4$), (♦) $M_1 : M_2 = 55 : 45$ ($M_n = 3.5 \times 10^4$), (▲) $M_1 : M_2 = 96 : 4$ ($M_n = 4.7 \times 10^4$), (●) $M_1 : M_2 = 98 : 2$ ($M_n = 1.9 \times 10^4$), and (■) $M_1 : M_2 = 100 : 0$ ($M_n = 4.1 \times 10^4$).

5 and **6**, when their thin films were allowed to contact with a neutral phosphate buffer solution (pH 7.5) at 27°C. The ordinate represents the ratio of the molecular weight of the remaining polymer after a specified time to the initial molecular weight. In both series, the heterogeneous hydrolysis became significantly slower as the content of M_2, having a hydrophobic benzyloxycarbonyl group, increased. The normalized curves of the molecular weight changes for copolyesters **5** and **6** in the spontaneous hydrolytic degradation lie between those for the corresponding two homopolymers. This means that the hydrolytic degradability can be controlled by the copolymer composition.

Spontaneous Hydrolysis Behavior of Copolyesters (9, 10) Having Pendant Carboxyl Groups

Removal of the benzyl groups of the two series of copolyesters **5** and **6**, by catalytic hydrogenolysis with palladium carbon, yielded the corresponding copolyesters (**9, 10**) having pendant carboxyl groups. The results are listed in Table III. The hydrogenolysis proceeded smoothly at room temperatures for copolyester **5**, whereas heating at 50°C was required for copolyester **6**. In the latter case, however, the hydrogenolysis was unavoidably accompanied by chain cleavage, although only to a slight extent.

Bn=CH2Ph

5, R=H
6, R=CO2 CH3

9, R=H
10, R=CO2 CH3
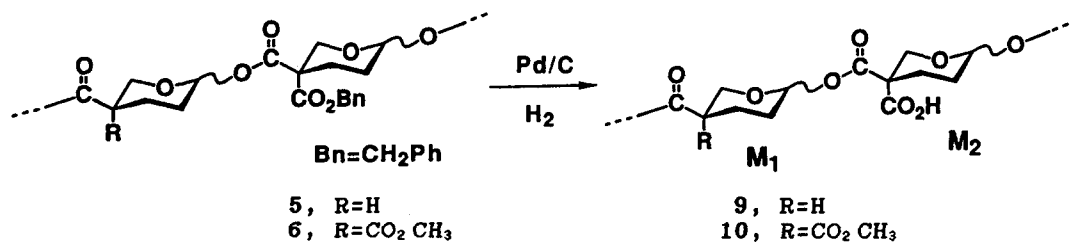
Figures 4 and 5 show the effect of the pendant carboxyl groups on the spontaneous heterogeneous hydrolysis of the copolyesters **9** and **10**, respectively, in a phosphate buffer solution (pH 7.5) at 27°C.

Introduction of only 3 mol % of the M_2 unit with a pendant carboxyl group to polyester **2** markedly accelerated the spontaneous hydrolysis, and copolyester **9** was completely degraded to low molecular

Table III Debenzylation of Copolyesters (5 and 6) Containing 4-benzyloxycarbonyl-2,6-dioxabicyclo[2.2.2]octan-3-one (4) Units

Copolyester (g)		Mol Frac. of 4 in Copolymer	Pd/C (mg)	Solv.[a] (mL)	Temp. (°C)	Time (h)	Yield (%)	$M_n^b \times 10^{-4}$
5	0.20	0.37	20	26[c]	15	18	91	1.4[d]
5	0.15	0.03	15	20	20	16	78	2.8
5	0.10	0.01	10	13	25	7	80	2.7
6	0.15	0.08	15	20	50	24	60	2.1
6	1.00	0.04	100	135	50	10	89	2.7
6	0.20	0.02	20	27	50	6	75	1.2

[a] Solvent, 1,4-dioxane.
[b] Determined by GPC (polystyrene standard).
[c] Solvent, dioxane-ethanol (3 : 2, v/v).
[d] Eluent, dimethyl sulfoxide; poly(8-oxa-6-azabicyclo[3.2.1]octan-7-one) standard.

weight compounds, soluble in the medium after the immersion for 21 days (Fig. 4). Similar, but lower, enhancement of the hydrolysis rate was observed for copolyester **10** with pendant methoxycarbonyl groups (Fig. 5). The higher the content of the M_2 unit with a carboxyl group, the faster the hydrolytic degradation of **10**.

In both series of copolyesters, **9** and **10**, a significant lowering of the molecular weight occurred in the initial stage of the hydrolysis. Since the hydrolysis was carried out in a buffer solution, the acceleration of the hydrolysis should be primarily ascribed to the increase of hydrophilicity, due to the introduction of the carboxyl groups. In a previous study,[11] we reported that polyesters (**11** and **12**), particularly the latter, having hydrophilic oligooxyethylene moieties in their side chains, were readily hydrolyzed under similar conditions.
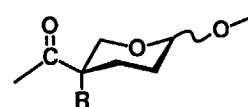
11, R=CO₂ CH₂ CH₂ OCH₃
12, R=CO₂ (CH₂ CH₂ O)₂ CH₃

Spontaneous Hydrolysis Behavior of Copolyesters (15) Containing 2,6-Linked Tetrahydropyran Rings

Previously, we investigated the cationic ring-opening polymerization of 6,8-dioxabicyclo[3.2.1]octan-7-one (**13**), an isomer of **1**, in detail, and clarified the specific polymerization behavior of this monomer[16-18]; the monomer **13** yielded polyester (**14**), consisting of a 2,6-linked tetrahydropyran ring, when the polymerization was carried out at or below
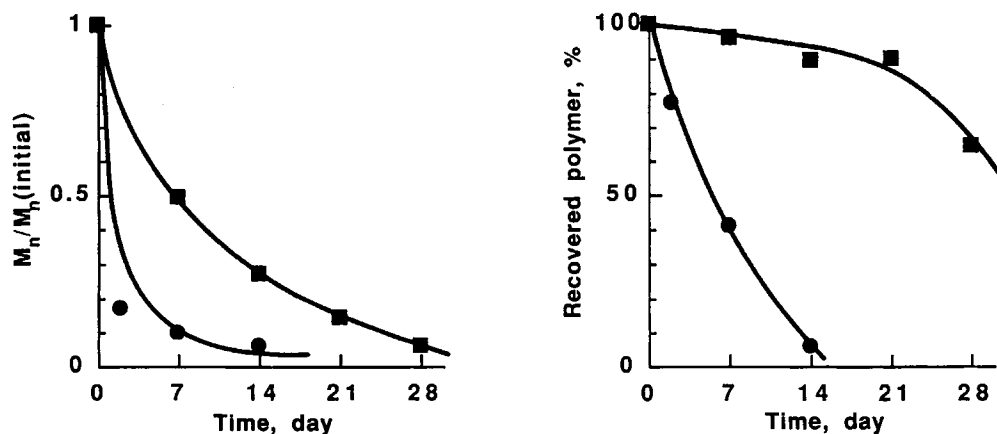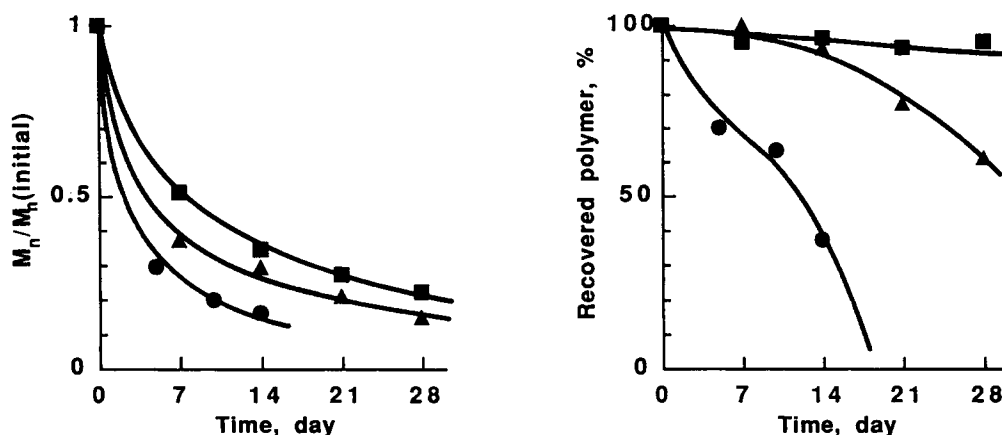

Figure 4 Changes in the molecular weight (left) and recovery of polymer (right) during the heterogeneous hydrolysis of copolyester 9 composed of unsubstituted (M_1) and carboxyl-substituted (M_2) tetrahydropyran units. Phosphate buffer, pH 7.5; temp., 27°C. (■) M_1 : M_2 = 100 : 0 (M_n = 3.5 × 10⁴), (●) M_1 : M_2 = 97 : 3 (M_n = 2.8 × 10⁴).

Figure 5 Changes in the molecular weight (left) and recovery of polymer (right) during the heterogeneous hydrolysis of copolyester **10** composed of methoxycarbonyl-substituted (M_1) and carboxy-substituted (M_2) tetrahydropyran units. Phosphate buffer, pH 7.5; temp., 27°C. (■) $M_1 : M_2 = 100 : 0$ ($M_n = 4.1 \times 10^4$), (▲), $M_1 : M_2 = 96 : 4$ ($M_n = 2.7 \times 10^4$), and (●), $M_1 : M_2 = 92 : 8$ ($M_n = 2.1 \times 10^4$).

−60°C and was terminated in the early stage. The prolonged reaction at −60°C, or the polymerization at a higher temperature, yielded only cyclic oligomers (10-membered cyclic dimer, 20-membered cyclic tetramer, and 25-membered cyclic pentamer).

13   **14**
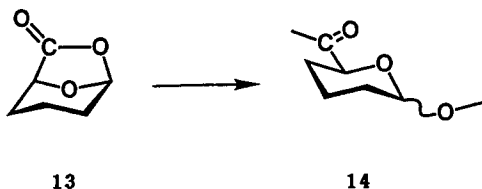
In the foregoing sections, we have described the effects of pendant groups on the spontaneous hydrolysis of polyesters, of which backbones are entirely consisting of 2,5-linked tetrahydropyran rings. In order to clarify the effect of the type of linkage

in the backbone on the spontaneous hydrolytic degradability, polyester **14**, composed of 2,6-linked tetrahydropyran rings, and copolyesters **15**, containing both 2,5-linked and 2,6-linked tetrahydropyran rings in their backbones, were prepared by cationic ring-opening polymerization of **13**, and copolymerization of **13** with **1**, respectively. The results are presented in Table IV.

15
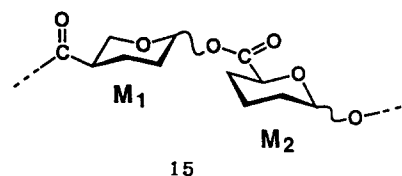
Spontaneous hydrolysis of the films of polyester **14** and copolyester **15** was tested in a phosphate

Table IV   Copolymerizaton of 2,6-dioxabicyclo[2.2.2]octan-3-one (1) with 6,8-dioxabicyclo[3.2.1]octan-7-one (13)

Mol Frac. of 13 in Feed	$[M]_0^a$ (mol/L)	Init.[b] (mol %)	Temp. (°C)	Time (min)	Yield (%)	Mol Frac. of 13 in Copolymer[c]	$M_n^d \times 10^{-4}$	$\dfrac{M_w^d}{M_n}$
1.00	2.6	2	−63	60	58	1.00	3.1	1.5
0.67	1.5	3	−60	120	32	0.39	1.0	1.9
0.40	1.5	1	−60	55	47	0.17	5.7	1.1
0.30	1.5	1	−60	20	68	0.03	6.7	1.1
0.00	1.0	2	−60	20	94	0.00	3.5	1.5

[a] Initial total monomer concentration; solvent, CH_2Cl_2.
[b] Initiator, BF_3OEt_2.
[c] Determined by ^1H-NMR.
[d] Determined by GPC (polystyrene standard).

buffer solution. As Figure 6 demonstrates, polyester 14 was more readily degraded than polyester 2. In fact, there remained no insoluble polymer in the former case after the films had been immersed in the buffer solution for 7 days. The hydrolytic degradability of copolymer 15 was found to fall between that for the two homopolyesters 2 and 14, that is, it increased with increasing content of the 2,6-linked structural units. This finding also suggests that the hydrolytic degradability of the polyester can be controlled by the incorporation of 2,6-linked tetrahydropyran units into the 2,5-linked tetrahydropyran polyester backbone by copolymerization.

Two model compounds, 16 and 17, for the structural units of 2 and 14, respectively, were prepared, and their hydrolysis rates were determined in a mixed solvent of methanold$_4$ and deuterium oxide (7 : 1, v/v) by monitoring the concentration of the substrate by ^{1}H–NMR spectroscopy. The mixed solvent was used, because 16 is not soluble in water, whereas 17 is soluble.

16   17
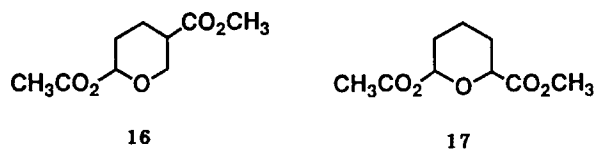
Since the hydrolysis was autoaccelerated by acetic acid that was liberated during the hydrolysis, the reaction rate was evaluated from the initial slope of

the logarithm of substrate concentration vs. time plots. The first-order rate constants were 6.0×10^{-7} s^{-1} for 16 and 1.4×10^{-7} s^{-1} for 17, respectively. The kinetic data indicate that the 2,5-disubstituted tetrahydropyran derivative 16 is more reactive than the 2,6-disubstituted tetrahydropyran derivative 17. Obviously, this is in conflict with the order of the hydrolytic degradability for polyesters 2 and 14, that is, 2,5-linked polyester 2 was less susceptible to hydrolysis than 14. Presumably, the discrepancy arises from the marked difference in the experimental conditions, that is, the homogeneous hydrolysis of the model compounds vs. the heterogeneous hydrolysis of the polyesters.

In heterogeneous hydrolysis, the hydrophilicity of the polyesters must be one of the most important factors. In order to evaluate the hydrophilicity of these two polyesters, 2 and 14, their films were allowed to stand for 2 weeks in a desiccator, in which the relative humidity was adjusted to 70–80%. The weight of the film of 14 increased up to about 1.4 times of the original weight by adsorption of moisture, whereas little weight increase was observed for the film of 2.

This observation, together with the aforementioned difference in solubility in water between the two model compounds 16 and 17, suggests that the molecular structure of 14 is more polar and, hence, more hydrophilic than that of 2. It would appear, therefore, that the higher susceptibility of the 2,6-linked polyester 14 to hydrolysis can be mainly as-
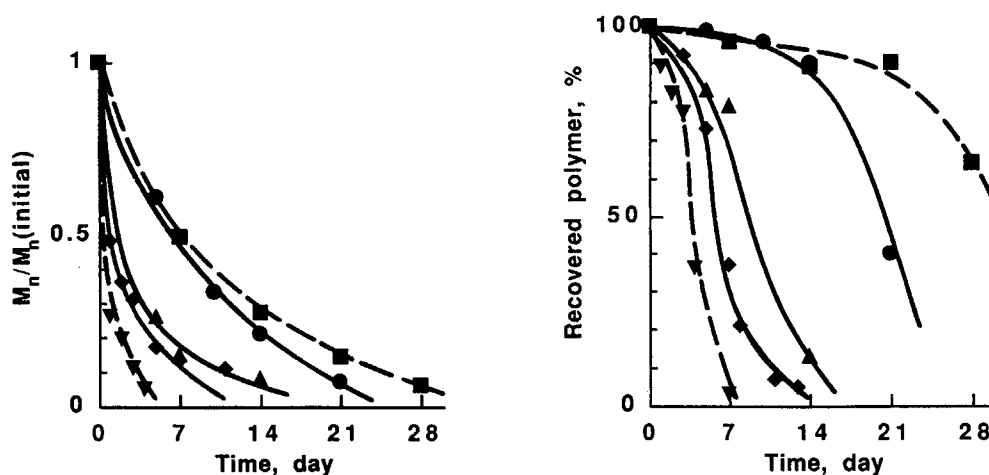

Figure 6   Changes in the molecular weight (left) and recovery of polymer (right) during the heterogeneous hydrolysis of copolyester 15 composed of 2,6-linked (M$_1$) and 2,5-linked (M$_2$) tetrahydropyran units. Phosphate buffer, pH 7.5; temp., 27°C. (■) M$_1$: M$_2$ = 100 : 0 (M$_n$ = 3.5 × 10^4), (●) M$_1$: M$_2$ = 97 : 3 (M$_n$ = 6.7 × 10^4), (▲) M$_1$: M$_2$ = 83 : 17 (M$_n$ = 5.7 × 10^4), (◆) M$_1$: M$_2$ = 61 : 39 (M$_n$ 1.0 × 10^4), and (▼), M$_1$: M$_2$ = 0 : 100 (M$_n$ = 3.1 × 10^4).

cribed to the higher hydrophilicity originating from its polar molecular structure, rather than to its chemical reactivity.

From the foregoing results, including the previously reported results,[11] the structural effects of these polyesters on the spontaneous hydrolytic degradability are summarized as follows:

1. Hydrophobic pendant ester groups retard the hydrolytic degradation, whereas carboxyl groups, as well as hydrophilic oligooxyethylene moieties, effectively accelerate it.

2. Polyester backbones, containing 2,6-linked tetrahydropyran rings, are more readily hydrolyzed than those entirely consisting of 2,5-linked tetrahydropyran rings.

3. Spontaneous hydrolytic degradability is widely varied by the copolymer composition of an appropriate combination of bicyclic lactones.

By taking these factors into consideration, we can design polyesters having controlled hydrolytic degradability for specific requirements. Biodegradability of these polyesters will be described in the succeeding article.[12]

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