NOTES

Synthesis and Biodegradation of Polyesters Based on *O*-Methylene Tartaric Acid

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Waste plastics are currently disposed of by either incineration, burying in landfills, or recycling. But most waste plastics disposed of in landfills are biologically inactive, so in such an environment these polymers that are not biodegradable will remain untouched and entombed indefinitely. Therefore, there is a growing demand for biodegradable plastics as a solution to problems concerning the global environment and plastic waste management.¹ Research on biodegradable plastics and polymers has been carried out worldwide with the aim of achieving harmony between human activity and the environment. Biodegradable polymers are classified² as (1) naturally occurring polymers constituting plants and animals, such as starch, cellulose, chitin, etc., (2) polymers produced in microorganism, such as poly(3-hydroxyalkanoate)s,³ pullulan,⁴ curdlan,⁵ poly(γ -glutamate),⁶ etc., and (3) chemically synthesized polymers, such as poly(ϵ -caprolactone),⁷ poly(ethylene glycol),⁸ poly(α -amino acid)s,⁹ etc. Among biodegradable synthetic polymers, aliphatic polyesters such as poly(lactic acid),¹⁰ poly(glycolic acid),¹¹ poly(butylolactone),¹² poly(ϵ -caprolactone),⁷ poly(butylene succinate),¹³ and their copolyesters are perhaps the most promising. One advantage of chemically synthesized biodegradable polymers is that their degradation rates can be controlled at will, so as to meet specific requirements by chemical modification of structure. Recently, polyesters having cyclic ethers such as tetrahydrofuran, tetrahydropyran, dianhydrohexitols and furan moieties have been reported to be biodegradable by Okada *et al.*¹⁴ These polyesters have been synthesized as carbohydrate- or quasi-carbohydrate-based polymers. The utilization of acyclic carbohydrate-based monomers such as glyceric acid¹⁵ and malic acid¹⁶ may give access to a class of biodegradable polymer.

L-Tartaric acid ((2*R*,3*R*)-(+)-2,3-dihydroxybutane dienoic acid) stands out as an easily accessible natural acyclic carbohydrate product. The synthesis of polymers from tartaric acid itself or its derivative has been reported for stereoregular polyamides¹⁷ and hydrolytically degradable poly(ester amide)s¹⁸ containing several chiral centers in their backbones. Polyesters from tartaric acid itself were investigated in the 1970s,¹⁹ and potential applications as controlled release agents have been studied in the last few years.²⁰ However, these polyesters were low molecular weight polymers because pendant functional groups such as hydroxyl groups participate in the polycondensation or subjected to

thermal degradation under severe conditions and then crosslinked polymers were easy to be formed.

The present article is concerned with the synthesis of novel polyesters having the dioxolane ring in the main chain by polycondensation of 2,3-*O*-methylene L or DL-tartaric acid dichlorides[L-MTC (**1a**) or DL-MTC (**1b**)] and different aliphatic diols, and their enzymatic degradation.

EXPERIMENTAL

Measurements

¹H NMR and ¹³C NMR spectra were obtained on a JEOL EX 270 spectrometer in CDCl₃ with tetramethylsilane as the internal standard. Infrared (IR) spectra were recorded on a HORIBA FT-210 spectrometer. Specific rotation was measured on a JASCO DIP-1000 spectropolarimeter at 25°C. Molecular weights were determined by gel permeation chromatography (GPC) using polystyrene calibration on a JASCO HPLC equipped with a Shodex KD-80M column at 40°C in CHCl₃. Thermal analysis was performed on a SEIKO SSC 5000 TG-DTA 200 thermal analyser at a heating rate of 10°C min⁻¹ for thermogravimetry (TG). Glass transition temperature was measured on a SEIKO SSC 5000 DSC 220 differential scanning calorimeter at a heating rate of 20°C min⁻¹ under nitrogen stream. The surfaces of films were observed with a scanning electron microscope (JEOL JSM-5300) after gold coating of the films using an ion coater.

Materials

L-Tartaric acid, DL-tartaric acid and paraformaldehyde were purchased from Kanto Chemicals Co. and used as received. Commercially available 1,2-ethylene glycol (**2a**), 1,4-butanediol (**2b**), and 1,6-hexanediol (**2c**) were purified by distillation under reduced pressure. Solvents used under anhydrous conditions were purified by distillation and dried by appropriate standard methods. The other

Scheme 1.

reagents and solvents were obtained commercially and used as received.

2,3-*O*-Methylene L and DL-tartaric acid (L-MTA and DL-MTA) were prepared by published method.¹⁷ 2,3-*O*-Methylene L and DL-tartaric acid dichlorides[L-MTC (**1a**) and DL-MTC (**1b**)] were synthesized by treating L-MTA and DL-MTA with thionyl chloride in the presence of catalytic amount of *N,N*-dimethylformamide (DMF) at 80°C for 10 h. The resulting mixture was concentrated and distilled under reduced pressure.

L-MTC (**1a**): 77% yield; bp 52°C [2 mmHg (0.27 k Pa)]; [α]_D^{26.0} +115° (c 1.0, in CDCl₃); IR (neat) 2973, 2915, 1804, 1508, 1134, 1022, 926, 835, 748 cm⁻¹; ¹H NMR (CDCl₃) 5.40 (s, 2H, methylene), 5.21 ppm (s, 2H, methine). DL-MTC (**1b**): 67% yield; bp 50°C [1.5 mmHg (0.2 k Pa)]; IR (neat) 2971, 2913, 1803, 1508, 1136, 1024, 925, 837, 748 cm⁻¹; ¹H NMR (CDCl₃) 5.40 (s, 2H, methylene), 5.21 ppm (s, 2H, methine).

Polycondensation

Polycondensation was carried out in a dry glass ampule equipped with a two-way stopcock under a dry N₂ atmosphere. To a stirred 5 mmol of aliphatic diols cooled at 0°C, 5 mmol of dichloride (**1a**) or (**1b**) were added in small portions. The mixtures were reacted first at normal pressure for 5 min at 0°C and allowed to reach room temperature under reduced pressure (*ca.* 50 mmHg) by an aspirator. These prepolymers were reacted at 120°C in the presence of titanium isopropoxide (0.5 mol%/monomer) under vacuum (1 mmHg) for 24 h. The polyesters prepared by the above method were further transesterified at 160°C under vacuum (1 mmHg) in the presence of titanium isopropoxide for 24 h. The resulting polyesters were isolated by dissolving the reaction mixtures in chloroform and pouring the solution into a large volume of methanol. They were purified by repeated reprecipitation using chloroform and methanol and dried *in vacuo*.

Enzymatic Degradation

The films (initial weights, ~5mg; initial dimension, 10 × 10 × 0.05 mm) cast from chloroform solution of polyesters were placed in small bottles with a screw cap to which a phosphate buffer solution of pH 7.4 (1 ml) and lipase (50 units) from porcine pancreas (Wako Pure Kogyo Co.) were added. The test bottles were incubated at 37 ± 0.3°C with shaking. Samples were periodically removed, washed with water and dried to constant weight in vacuum. As blank tests, test bottles containing only either the sample or the enzyme were shaken under the same conditions.

RESULTS AND DISCUSSION

Although L-MTA and DL-MTA appeared unstable toward strong acids such as hydrochloric acid, L-MTC (**1a**) and DL-MTC (**1b**) could be synthesized in moderate yields by reactions of L-MTA and DL-MTA with thionyl chloride in the presence of a small amount of DMF. **1a** and **1b** could be purified by distillation *in vacuo*.

Polycondensations of dichlorides **1a** and **1b** with different aliphatic diols **2a**, **2b** and **2c** were carried out in bulk, first at normal pressure for 5 min at 0°C, and

Table I. Polycondensations of 2,3-*O*-methylene tartaric acid dichlorides with aliphatic diols^a

Run	Monomer			Yield %	$\bar{M}_n^c$ 10 ⁴	$\bar{M}_w/\bar{M}_n^c$	[α] _D ^d degree
	Diacid chloride	Diol	Polyester				
1	1a	2a	3a	80	0.25	2.3	-72.1
2 ^b	1a	2a	3a	82	0.31	2.1	-7.24
3	1b	2a	3b	92	0.18	1.9	0
4 ^b	1b	2a	3b	90	0.24	1.8	0
5	1a	2b	3c	90	0.83	2.1	-82.2
6 ^b	1a	2b	3c	93	1.55	1.9	-82.2
7	1b	2b	3d	91	0.80	2.0	0
8	1a	2c	3e	98	1.62	1.7	-80.0
9	1b	2c	3f	95	0.75	1.9	0
10 ^b	1b	2c	3f	96	2.11	1.6	0

^a Polycondensation was carried out in bulk at 120°C/1 mmHg for 24 h as described in the experimental section. ^b The polyesters of Runs 1, 3, 5, and 9 were transesterified in the presence of titanium isopropoxide (0.5 mol%) at 160°C/1 mmHg for 24 h. ^c Determined by GPC on the basis of polystyrene calibration. ^d Measured in chloroform at 25°C.

then under vacuum (1 mmHg) in the presence of titanium isopropoxide (0.5 mol%) at 120°C for 24 h. The pre-polyesters prepared at 120°C, 1 mmHg for 24 h were further transesterified at 160°C, 1 mmHg for 24 h. Some of the results on the polycondensation are shown in Table I. The polyesters with molecular weights up to 2.1×10^4 were obtained in high yields. The molecular weights of these polyesters were estimated by gel permeation chromatography (using polystyrene standards). The transesterification method resulted in increasing molecular weight of polyesters without side reaction such as crosslinking. Polycondensation of dimethyl esters of L-MTA or DL-MTA with **2b** was also carried out in bulk in the presence of titanium isopropoxide as a catalyst at 140°C. However, only crosslinked polyester were obtained. This may be due to the formation of hydroxyl groups in polymer side chains by transmetalization reactions of L-MTA dimethyl ester and free methanol or **2b** at high temperature. Solution polycondensation of L-MTC and **2b** was also done in a mixed solvent of pyridine and chloroform at 40°C, but the molecular weight of the resulting polyester **3c** was not improved. As can be seen from Table I, reactions using diols **2b** and **2c** gave the polyesters with high molecular weights, while the reaction using diol **2a** resulted in polyesters of number average molecular weight up to three thousand and viscous oily polymers. All polyesters from **1a** and different diols showed negative optical rotations, although **1a** as monomer showed positive optical rotation. The optical rotations of all polyesters were almost independent of carbon number of aliphatic diols used and seemed little affected by the density of chiral centers in the backbone.

The structures of polymers were characterized by ¹H NMR and ¹³C NMR, IR, DSC, and TGA methods. The infrared spectra of polyesters exhibited characteristic absorptions at 1741 (C=O stretching) and 1236 (C–O–C stretching in ester bond), 1116, 1064, and 919 cm⁻¹ (C–O–C stretching in dioxolane ring). Both ¹H NMR and ¹³C NMR spectra displayed sharp signals whose chemical shifts and intensities were consistent with the

Figure 1. ^1H and ^{13}C NMR spectra of polyester 3c.

microstructures expected for these polyesters (Figure 1). In particular, well-resolved singlets were observed in ^1H NMR spectra for the two protons attached to the respective asymmetric backbone carbon atoms and the ^{13}C NMR spectra for the two carbonyl groups contained in the repeating units. It may be concluded, therefore, that the occurrence of tartaric moieties in the meso configuration which seemed to arise by racemization, should be considered negligible in these polyesters. No significant differences in chemical shifts of ^1H NMR and ^{13}C NMR spectra were observed between optically active polyesters and the corresponding optically inactive polyesters.

The thermal properties of the polymers were examined by TG and DSC analyses in nitrogen atmosphere. Decomposition temperatures (T_d s), melting temperatures (T_m s) and glass transition temperatures (T_g s) of the polyesters are summarized in Table II. Since polyesters **3a** and **3b** were viscous oily polymers, T_g s and T_m s of these polyesters were not detected. Optically active polyesters exhibit 11–17°C higher T_d s, 2–4°C higher T_m s and 2–3°C higher T_g s compared with racemic polyesters. These results suggest that the optically ac-

Table II. Thermal properties of polyesters 3

Polyester	T_g^a	T_m^a	ΔH_m^a	T_d^b
	°C	°C	J g $^{-1}$	°C
3a	ND ^c	ND ^c	—	301
3b	ND ^c	ND ^c	—	290
3c	–5	81(104) ^d	40(33) ^d	320
3d	–8	79(100) ^d	8(32) ^d	303
3e	–22	78	35	329
3f	–24	76	37	318

^a Determined by DSC in nitrogen at a heating rate of 10°C min $^{-1}$. ^b T_d is the temperature of 10% weight loss, measured by TG in nitrogen at 10°C min $^{-1}$. ^c Not detected. ^d Two peaks were observed.

tive polyesters possess higher order structures than the corresponding inactive polyesters. In DSC thermograms the melting points of polyesters **3e** and **3f** are defined by a single endotherm at about 78°C, while for the case of polyesters **3c** and **3d**, two peaks at about 80 and 104°C are systematically observed but only that one appearing at higher temperature was found when the molten

Figure 2. Enzymatic degradation profiles of polyesters by porcine pancreas (pH 7.4, 37°C). □, 3c; ■, 3d; ○, 3e; ●, 3f; ▲, 3e without lipase.

Figure 3. SEMs of the surfaces of 3e films before (A) and after (B) enzymatic degradation for 3 days by porcine pancreas.

sample was cooled down to room temperature and slowly reheated. The enthalpy of fusion (ΔH_m) of optically active polymer 3c for peak appearing at lower temperature was about five times that of inactive polyester 3d. Since double melting has been interpreted as due to the fusion of different sizes of crystallites,²¹ it is suggested that polyesters 3c and 3d possess two crystallites differing in size. Solubility experiments showed that all the polyesters were soluble in chlorinated hydrocarbons, dimethyl sulfide, dimethylformamide and tetrahydrofuran.

Although evaluation of biodegradation of the polymer by a certain enzyme was not necessarily reflected exactly on the biodegradability in environments such as soil, activated sludge, and seawater, we investigated the enzymatic degradation of the present polyesters by lipase from porcine pancreas as a guide of the biodegradation in natural environments. The enzymatic degradation of the polyesters was carried out with solution-cast films (initial weight, 3–5 mg) at 37°C in a 0.1 M phosphate buffer (pH 7.4) using lipase from porcine pancreas. Figure 2 shows the results of enzymatic degradation on polyesters 3c, 3d, 3e, and 3f. As clearly seen in Figure 2, optically active polyester 3e was degraded the fastest. After 6 days, it was nearly completely degraded, while the corresponding optically inactive polyester 3f was little degraded. In contrast, for optically active polyester 3c, approximately 50 wt% of the original sample was degraded after 6 days, but the corresponding optically inactive polyester 3d was scarcely degraded. Therefore, the degradability of the dioxolane ring-containing polyesters derived from tartaric acid by porcine pancreas lipase seemed considerably affected by stereochemistry and chemical constituents. Differences in enzymatic degradability of 3c and 3e may arise from their crystallinities, since the enthalpy of fusion (ΔH_m) of 3c exhibited larger value than that of 3e (Table II). Figure 3 shows the scanning electron micrographs (SEMs) of the surfaces of polyester 3e films before and after the enzymatic degradation for 3 days. The surface of the degraded polyester film is apparently blemished by the action of porcine pancreas lipase. These observations suggest that the polyesters derived from 2,3-O-methylene L-tartaric acid and aliphatic diols are biodegradable.

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