Molecular Design of Photocurable Liquid Biodegradable Copolymers. 1. Synthesis and Photocuring Characteristics

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ABSTRACT: Photocurable liquid biodegradable copolymers were prepared by ring-opening copolymerization of ϵ-caprolactone (CL) and trimethylene carbonate (TMC) at an equimolar monomer feed ratio in the presence of a polyol as an initiator and tin(II) 2-ethylhexanoate as a catalyst, followed by subsequent coumarin derivatization at their hydroxyl terminus. These liquid copolymers (molecular weight range from approximately 2500 to 12 000), tri- and tetracoumarinated copolymers, were cross-linked by ultraviolet (UV) light irradiation. Photocuring was enhanced by higher coumarin functionality, higher UV intensity, and reducing the thickness of the liquid film precursor. Stereolithographically prepared microarchitectured surfaces were demonstrated for potential applications in biomedical fields.

photocuring, liquid copolymer, ϵ-caprolactone, trimethylene carbonate, coumarin

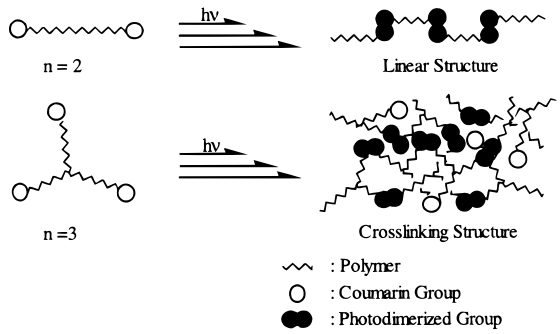
Introduction

Although biodegradable polymers have been popular as biomaterials, they are solids;[1] to construct a scaffold for tissue engineering or for devices, fabrication processes such as spinning, casting, or molding of these materials are required. On the other hand, few studies have dealt with liquid biodegradable polymers. If a liquid biodegradable polymer can be transformed from a liquid to a solid state by photoirradiation, such functional materials may find versatile biomedical applications such as in photochemically driven wound-healing materials, photofabrication of drug delivery devices, photofabrication of computer-assisted-design-(CAD-) based microarchitectured devices and surface coatings of implanted devices.

To this end, a preparation of photochemically active biodegradable liquid copolymers was carried out in this paper. As a photoreactive center, a photodimerizable coumarin group was incorporated into the chain ends of biodegradable liquid copolymers. Since intermolecular association of a pair of associated coumarin groups results in the formation of a photodimer upon ultraviolet (UV) light irradiation, chain extension and cross-linking of liquid multifunctional polymers may induce a liquid-to-solid-phase transformation (Scheme 1). As liquid biodegradable polymers, we prepared a series of copolymers composed of ϵ-caprolactone (CL) and trimethylene carbonate (TMC) with different molecular weights and different functionality (di-, tri-, and tetrabranched) on an equimolar basis.[2]

In this paper, the preparation of photoreactive biodegradable liquid copolymers and dependence of their photocuring characteristics on molecular parameters and operational conditions were studied. As examples for biomedical applications, stereolithographically microprocessed surfaces, which were prepared via liquid-to-solid-phase transformation induced by photoirradiation, were demonstrated.

Scheme 1. Photopolymerization of Coumarinated Copolymers



Experimental Section

General Procedure. All the solvents and reagents were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan) or Sigma-Aldrich Japan, Inc. (Tokyo, Japan). Diglycerol poly(oxyethylene glycol ether) (b-PEG) was obtained from Shearwater Polymers, Inc. Trimethylene carbonate (TMC) was recrystallized from a mixed solvent of ethyl acetate and hexane. Trimethylolpropane and Pentaerythritol were recrystallized from acetone. Other solvents and reagents were purified by distillation. ^{1}H NMR spectra were recorded on a JEOL JNM-GX270 FT-NMR spectrometer (270 MHz, Tokyo, Japan). The chemical shifts were given as δ values from Me_4Si as the internal standard. IR spectra were recorded on a Shimadzu DR-8020 FT-IR spectrophotometer (Kyoto, Japan). UV absorption spectra were recorded on a JASCO Ubest-30 UV/vis spectrophotometer (Tokyo, Japan). The molecular weights of the polymers were determined by GPC analysis, which was carried out on a Toso SC-8020 (Tokyo, Japan). UV light (250 W Hg−Xe lamp: Hamamatsu Photonics L5662−02, Shizuoka, Japan) was irradiated through a Pyrex filter. The intensity of the UV light source was measured at 250 nm on a TOPCON UVR-25 (Tokyo, Japan). The surface observa-

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tion of photocured films by scanning electron microscopy (SEM) was carried out on a JEOL JSM-6301F (Tokyo, Japan).

Synthesis of Trimethylene Carbonate (TMC) (1). The preparation of TMC was carried out according to a method reported previously.[2] Briefly, a piece of sodium (3.2 g, 0.14 mol) was dissolved in 60 mL of ethanol, and the solution was mixed with 1,3-propanediol (362 mL, 4.99 mol) and diethyl carbonate (665 mL, 5.5 mol). The reaction mixture was stirred overnight at room temperature under N_2 atmosphere, and then ethanol was removed by evaporation. The crude product was dissolved in 1.5 L of toluene, and anhydrous magnesium sulfate was added to this cloudy solution. The suspension was allowed to stand overnight at room temperature. After filtration of the mixture, filtered toluene was removed by evaporation, and **1** was collected by distillation under reduced pressure. The yield was 350.0 g (68.8%). Mp: 46.5 °C. FT-IR (KBr, cm^{-1}): 3000, 2940, 1744, 1255, 1164, and 1120. ^1H NMR (270 MHz, $CDCl_3$, ppm): $\delta = 2.12$ (2H, quintet, $J = 5.4$ Hz), and 4.42 (4H, triplet, $J = 5.4$ Hz).

Synthesis of 7-Ethoxycarbonylmethoxycoumarin (5). A mixture of 7-hydroxycoumarin (20.26 g, 125 mmol), potassium carbonate (24.7 g, 179 mmol), ethyl bromoacetate (25.0 g, 150 mmol), and dry acetone (450 mL) was refluxed for 2 h while stirring in a N_2 atmosphere. After removal of salt by filtration, the resulting **5** was recrystallized from ethanol. The yield was 27.7 g (89%). ^1H NMR (270 MHz, DMSO-d_6, ppm): $\delta = 1.18$ (3H, triplet, $J = 8.1$ Hz), 4.16 (2H, quartet, $J = 8.1$ Hz), 4.91 (2H, singlet), 6.28 (1H, doublet, $J = 9.9$ Hz), 6.96 (1H, doublet, $J = 2.0$ Hz), 6.98 (1H, quartet, $J = 2.0$, and 8.9 Hz), 7.61 (1H, doublet, $J = 8.9$ Hz), 7.96 (1H, doublet, $J = 9.9$ Hz).

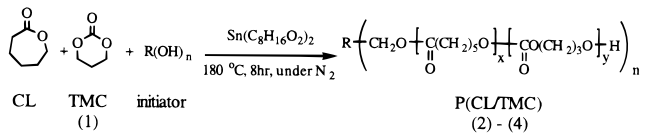
Synthesis of 7-Carboxymethoxycoumarin (6). A mixture of **5** (6.92 g, 27.9 mmol) and 1,4-dioxane (280 mL) was mixed with sodium hydroxide aqueous solution (16.2 g NaOH, 405 mmol) in 400 mL of distilled water and was stirred overnight at room temperature. After acidification of the solution (with hydrochloric acid), organic substances were extracted with a chloroform/methanol mixed solvent. The solvents were removed by distillation under reduced pressure. The resulting **6** was isolated by recrystallization from ethanol. The yield was 5.51 g (90%). ^1H NMR (270 MHz, DMSO-d_6, ppm): $\delta = 4.83$ (2H, singlet), 6.28 (1H, doublet, $J = 9.9$ Hz), 6.95 (1H, doublet, $J = 2.0$ Hz), 6.97 (1H, doublet, $J = 2.0$, and 8.9 Hz), 7.62 (1H, doublet, $J = 8.9$ Hz), 7.97 (1H, doublet, $J = 9.9$ Hz), 13.13 (1H, s).

Synthesis of 7-Chlorocarbonylmethoxycoumarin (7). A mixture of **6** (3.76 g, 17.1 mmol) and thionyl chloride (20.0 mL 277 mmol) was refluxed for 3 h while being stirred in a N_2 atmosphere. After removal of the unreacted thionyl chloride by distillation, **7** was obtained. The yield was 4.00 g (98%). ^1H NMR (270 MHz, DMSO-d_6, ppm): $\delta = 4.83$ (2H, singlet), 6.28 (1H, doublet, $J = 9.9$ Hz), 6.94(1H, doublet, $J = 2.0$ Hz), 6.96 (1H, quartet, $J = 2.0$, and 8.9 Hz), 7.62 (1H, doublet, $J = 8.9$ Hz), 7.97 (1H, doublet, $J = 9.9$ Hz).

Synthesis of Poly(ϵ-caprolactone-*co*-trimethylene carbonate) Copolymer (Poly(CL/TMC)). A typical procedure for the preparation is as follows. A reaction mixture of 0.33 M tin(II) 2-ethylhexanoate solution in toluene (125 μL, 43 μmol), trimethylolpropane (TMP) (4.38 g, 32.6 mmol), **1** (64.0 g, 627 mmol), and ϵ-caprolactone (CL) (71.8 g, 629 mmol) was stirred for 8 h at 180 °C in a N_2 atmosphere. After vacuum distillation of unreacted monomers, the copolymer, poly(CL/TMC) (**3b**), was isolated by precipitation in methanol. The yield was 139.0 g (99%). $M_n = 8140$ (determined by GPC; eluent, DMF). FT-IR (KBr, cm^{-1}): 3529, 2955, 2866, 1744, 1252, 1164, and 1036. ^1H NMR (270 MHz, $CDCl_3$, ppm): $\delta = 1.37$ (multiplet), 1.62 (multiplet), 2.01 (multiplet), 2.27 (multiplet), 3.68 (multiplet), and 4.20 (multiplet).

Synthesis of Coumarin End-Capped Poly(CL/TMC). A typical procedure for the preparation is as follows. A mixture of **3b** (20.4 g, 2.51 mmol) and **7** (6.14 g, 25.7 mmol) was stirred for 3 h at 80 °C in a N_2 atmosphere. The resulting coumarin end-capped copolymer (**3b**) was isolated by precipitation in methanol. The yield was 17.8 g (82%). Coumarin content = 3.50×10^{-4} mol/g. Molecular weight (based on coumarin content, described below) = 8500. FT-IR (KBr, cm^{-1}): 2953, 2866, 1743, 1614, 1250, 1164, and 1036. ^1H NMR (270 MHz, $CDCl_3$, ppm): $\delta = 1.37$ (multiplet), 1.62 (multiplet), 2.01 (multiplet), 2.27 (multiplet), 4.20 (multiplet), 4.69 (multiplet), 6.26 (doublet, $J = 9.3$ Hz), 6.79 (doublet, $J = 2.4$ Hz), 6.87 (quartet, $J = 2.4$, and 8.3 Hz), 7.39 (doublet, $J = 8.3$ Hz), and 7.62 (doublet, $J = 9.3$ Hz).

Scheme 2. Preparation of Biodegradable, Liquid Copolymer



Determination of the Coumarin Content of Copolymers. The UV spectrum was recorded for a solution with coumarin end-capped copolymer dissolved in 1,4-dioxane. The coumarin content of grafted copolymer (number of coumarin per weight) was determined using an ϵ_{max} of 1.35×10^4 (318 nm). The molecular weight of grafted copolymer was calculated from multipling the inverse of coumarin content with number of graft chain per molecule.

Photocuring Characteristics. Each coumarin end-capped copolymer, coated on a cover glass, was irradiated with UV light. After immersion into dichloromethane, the insoluble copolymer was weighed. The photocuring yield was defined as the weight percentage of the insoluble part (W_g) against that of the coated copolymer (W): $W_g/W \times 100$.

Water Adsorptivity. Each photoirradiated film of the coumarin end-capped copolymer (ϕ 15 and 0.3 mm thickness) was immersed in water for 2 days at room temperature. The degree of water adsorptivity (DW) was determined as the relative amount of water uptake against the copolymer.

Stereolithographic Apparatus (SLA). The SLA was custom-designed and composed of a moving light pen (diameter, 1 mm), an optical fiber which connected the light pen and a UV light source (Hg−Xe lamp), a fixed sample holder, and a stage controller (Sigma Koki MARK-41, Tokyo, Japan) driven by a personal computer. The stage controller manipulated movement of the light pen. The round cover glass was coated with a thin layer of poly(2-(7-coumaryloxy)ethyl methacrylate-*co*-dimethyl acrylamide) which was donated by Dr. Nakayama (National Cardiovascular Center, Osaka, Japan), and subsequently fully photoirradiated to yield a highly cross-linked coumarinated surface. The liquid photoreactive copolymer prepared in this study was used to coat this coumarinated cover glass (thickness, 0.05 mm). Then, under photoirradiation via the light pen, the moving stage was moved rectangularly at a speed of 0.6 mm/min. The liquid refilling on the surface and the subsequent photoirradiation was repeated over 10 cycles. After the sample was washed with dichloromethane, SEM observation was carried out.

Results

Preparation of Photoreactive Poly(CL/TMC) Copolymers. Scheme 2 illustrates the ring-opening copolymerization of ϵ-caprolactone (CL) and trimethylene carbonate (TMC) at an equimolar monomer feed composition in the presence of polyol (trimethylene glycol, trimethylolpropane, Pentaerythritol, or diglycerol poly(oxyethylene glycol ether) (b-PEG)) as an initiator (detail of the structure is shown in Table 1) and tin(II) 2-ethylhexanoate as a catalyst. Copolymers (poly(CL/TMC)) with different molecular weights and different numbers of terminal hydroxyl groups were obtained. According to Scheme 2, copolymerization initiated with diol, triol, and tetraol produce linear copolymers, tribranched copolymers, and tetrabranched copolymers, respectively, in which each terminus has one hydroxyl group. Irrespective of the type of copolymer, the yield was almost 100 percent. All the resulting copolymers

Table 1. Biodegradable Liquid Copolymers

	noncoumarinated copolymer					coumarin end-capped copolymer		
	initiator							
polymer	$R(CH_2OH)_n$	n[a]	fraction[b]	M_n[c]	CL:TMC[d]	content[e] (mol/g)	M_w[f]	DW[g]
2a	$CH_2(CH_2OH)_2$	2	6.6	2200	0.50:0.50	8.02×10^{-4}	2500	
2b	$CH_2(CH_2OH)_2$	2	13.2	4300	0.49:0.51	3.40×10^{-4}	5900	
3a	$CH_3CH_2C(CH_2OH)_3$	3	6.6	2900	0.51:0.49	8.10×10^{-4}	3700	0.03
3b	$CH_3CH_2C(CH_2OH)_3$	3	13.2	8100	0.50:0.50	3.50×10^{-4}	8500	0.03
3c	$CH_3CH_2C(CH_2OH)_3$	3	20.4	12000	0.50:0.50	3.00×10^{-4}	10000	0.02
4a	$C(CH_2OH)_4$	4	6.6	5300	0.49:0.51	7.90×10^{-4}	5100	0.03
4b	$C(CH_2OH)_4$	4	13.2	13000	0.50:0.50	3.39×10^{-4}	12000	0.02
4c	b-PEG[h]	4	6.6	7400	0.49:0.51	5.71×10^{-4}	7000	0.58

[a] Multifunctionality of initiator. [b] Molar fraction of monomer per total number of OH groups. [c] Number-average molecular weight determined by GPC (PEO Standard). [d] Copolymer composition of PCL/PTMC. [e] Quantities of coumarin moieties in the coumarinated copolymer calculated by UV measurements. [f] Molecular weight determined based on coumarin content. [g] Degree of water adsorptivity (relative weight of water uptake by the polymer). [h] Branched-PEG (diglycerol polyoxyethylene glycol ether) (MW 2040) purchased from Shearwater, Inc.:

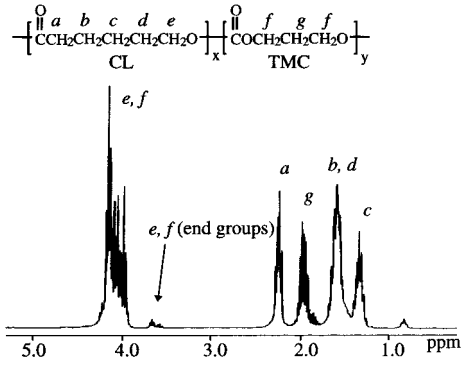


Figure 1. ^1H NMR spectrum (270 MHz) of copolymer **3b** in $CDCl_3$.

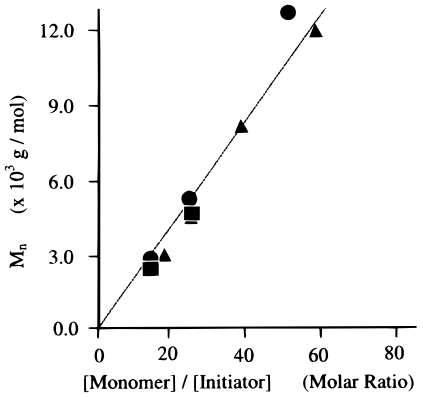


Figure 2. Molecular weights of copolymers **2** (■), **3** (▲), and **4** (●) under different molar ratios of monomer to initiator.

were viscous liquids. Table 1 summarizes the reaction conditions and the compositions and the molecular weights of the copolymers. The compositions of the copolymers, as determined by ^1H NMR spectroscopy (Figure 1), were almost equimolar as expected. The molecular weight of the copolymers ranged from 2200 to 13 000, depending on the molecular ratio of the monomer to the hydroxyl groups of the initiator, as well as functionality of the initiator. Figure 2 shows that the molecular weight of a copolymer increases linearly with an increase in the molar ratio of monomer to hydroxyl groups, irrespective of the functionality of alcohol.

Coumarin end-capped copolymers were prepared by esterification of hydroxyl end groups with an acid chloride derivative of coumarin (**7**) at different concentrations of acid chloride, as shown in Scheme 3. After precipitation to remove unreacted **7**, UV spectral measurements in 1,4-dioxane solution at 318 nm, which is the wavelength of a characteristic peak of the coumarin group, were carried out. As shown in Figure 3, the intensity increased linearly with an increase in the weight ratio of **7** to copolymer at low feed ratios and remained constant at higher ratios. The molecular weights calculated based on the coumarin content of the copolymers, which were determined from the value at full endcapping with coumarin at a high molar ratio of **7** to copolymer, as shown in Figure 3, were approximately similar to those of the noncapped copolymers.

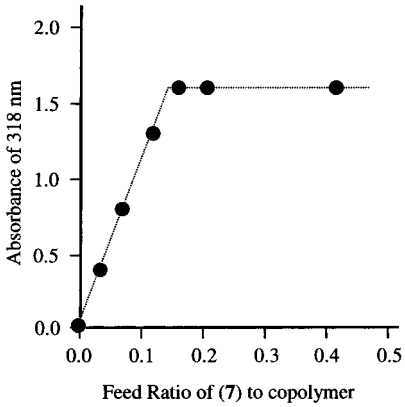
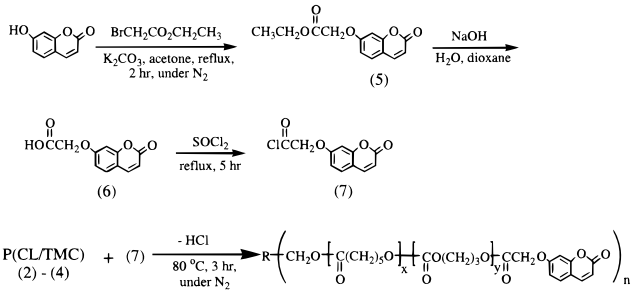


Figure 3. UV absorbance of copolymer **3b** in 1,4-dioxane (1.5 g/L) at 318 nm as a function of weight feed ratio of coumarin derivative **7** to copolymer.

Scheme 3. Preparation of Photoreactive, Biodegradable, Liquid Copolymer



Photocuring Characteristics. The photodimerization reaction using a Hg−Xe lamp was carried out in a liquid film obtained by casting from the dichloromethane solution of a photoreactive copolymer on a glass plate

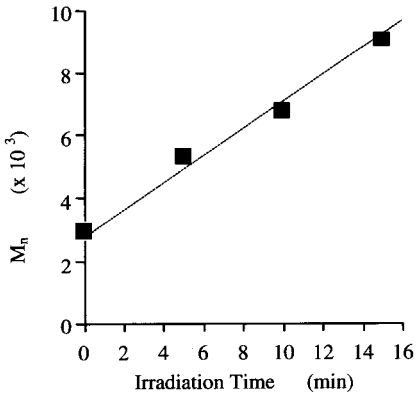


Figure 4. Number-average molecular weight (M_n) of difunctional coumarin end-capped copolymer (**2b**) (■) film under UV irradiation. Film thickness: 0.03 mm. UV intensity: 10.8 mW/cm^2.

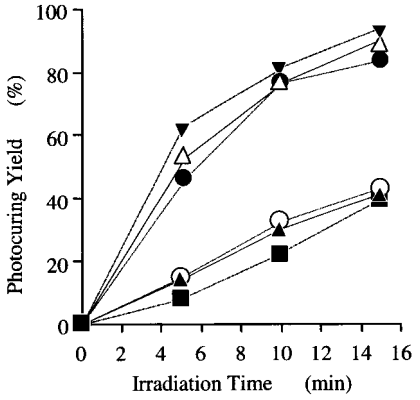


Figure 5. Time-dependent photocuring yield of coumarin end-capped copolymers **3a** (▲), **3b** (○), **3c** (■), **4a** (▼), **4b** (△), and **4c** (●) films under UV irradiation. Film thickness: 0.03 mm. UV intensity: 10.8 mW/cm^2.

and subsequent evaporation at room temperature. The coumarin end-capped photocured copolymers, derived from linear copolymers (**2a** and **2b**) initiated with trimethylene glycol, were soluble in dichloromethane. The molecular weights of the photocured copolymers increased linearly with photoirradiation time (Figure 4). On the other hand, tri- and tetrafunctionalized coumarin end-capped copolymers produced cross-linked copolymers which were not soluble in any organic solvent. The photocuring yield (nonsoluble part of a photocured copolymer) increased with photoirradiation time (Figure 5). Tetrabranched copolymers had much better photocuring characteristics than tribranched ones. No significant dependence of the photocuring rate on the molecular weight of the photoreactive copolymers was observed among photoreactive copolymers with the same functionality. As shown in Figure 6, photocuring was more effective with thinner liquid films (0.01 mm thickness) than with thicker ones (0.03 mm). The UV-intensity dependence of photocuring is shown in Figure 7. An increase in photointensity significantly increased photocuring rate. The initial photocuring rate, determined from the slope during the early period of photoirradiation in Figure 7, increased linearly with photointensity (Figure 8).

All the photocured films were rigid solids. Upon immersion in water, little swelling occurred. Only a small percentage of water on the weight basis of the photocured film was absorbed by the photocured copolymers. Photocured films of **4c**, which were based on b-PEG, exhibited a higher swelling tendency than others.

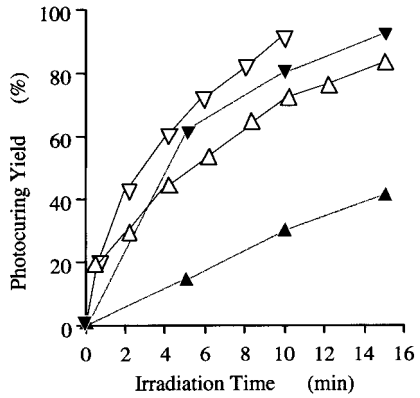


Figure 6. Time-dependent photocuring yield of coumarin end-capped copolymers **3a** (▲ and △) and **4a** (▼ and ▽). Film thickness: (▲ and ▼) 0.03 mm; (△ and ▽) 0.01 mm. UV intensity: 10.8 mW/cm^2.

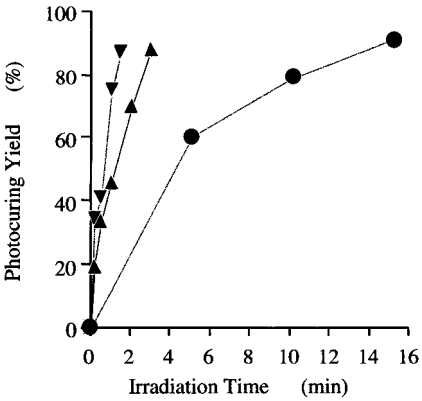


Figure 7. Time-dependent photocuring yield of coumarin end-capped copolymer **4a** film at UV intensities of 10.8 (●), 50.6 (▲), and 100.2 (▼) mW/cm^2. Film thickness: 0.03 mm.

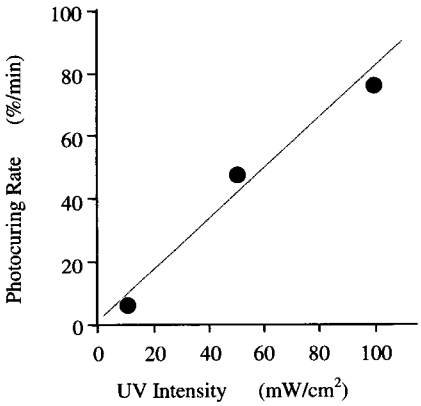


Figure 8. Relationship between photocuring rate and UV intensity. Photoreactive copolymer: **4a** (●). Film thickness: 0.03 mm.

Photofabrication of Microarchitectured Surface. A microarchitectured surface was prepared by repeated cycles of coating of a liquid photoreactive copolymer and subsequent UV light irradiation. These procedures were semiautomatically manipulated with a custom-designed, laboratory-scale stereolithographic apparatus (SLA) equipped with computer-assisted design (CAD). The repeated cycles of photoirradiation via the moving light pen on a liquid film of the biodegradable photoreactive copolymer (**4a**), poured onto a fully

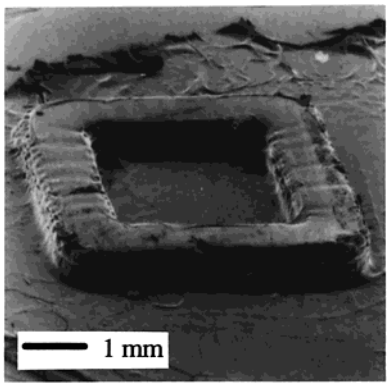


Figure 9. SEM Image (×10) of a stereolithographic microstructure of **4a** on a coumarinated cover glass.

coumarinated and photocured copolymer, produced a stereolithographic microstructure (approximately 0.5 mm high, 1.0 mm wide and 4.0 mm long) on the surface as shown in Figure 9. The coumarinated primer used enables us to provide high coumarin density at the surface region, which react with coated coumarinated poly(CL/TMC), resulting in formation of covalent bonding to ensure interfacial adhesion strength.

Discussion

Photocurable substances can be used for wound-healing materials such as in tissue adhesive sealants or tissue adhesion prevention, the matrix of drug delivery devices, the surface coating for implanted devices, and microarchitectured devices when a liquid prepolymer or polymer can be solidified by photoirradiation. The designed photoreactive prepolymers or polymers would have photoreactive centers in their molecules. To this end, we are developing a photochemical processing technology and molecular designs of photoreactive biomaterials leading to either cross-linking or polymerization resulting in photoinduced liquid-to-solid transformation. The photoreactive centers used in our previous studies are photodimerizable groups inducing a [2 + 2] cycloaddition reaction[3,4] and photochemical-radical generating groups such as benzophenone,[4] arylazido,[5] dithiocarbamate,[6] and xanthene dyes.[7] In the latter case, highly reactive radical species produced by photolysis induce complex radical reactions including proton withdrawal, radical recombination, and initiation of polymerization in the presence of vinyl monomers.

Previously used photodimerizable groups include cinnamate,[3] thymine, and coumarin.[4] The advantage of the photodimerization groups in this particular application is that the reaction proceeds only between a pair of groups in an associated state. This enables immobilization of biologically active substances into photocured matrices with minimal adverse effects on immobilized substances and no need for the removal of unreacted cross-linking agents remaining in the photocured matrices. This totally prevents any leaching or loss of immobilized substance as opposed to conventional cross-linking techniques. In fact, multifunctionally derivatized substances produced photocured films and microspheres within which bioactive substances were immobilized in biologically derivatized substances such as hyaluronate or gelatin or in synthetic hydrophilic polymers.[3−8]

Our synthetic design strategy for novel photochemically driven functional biomaterials for fabrication of devices, surface layering, and drug immobilization, all of which should be biodegradable, consists of the liquid biodegradable copolymer multifunctionally end-capped with coumarin groups. As for a biodegradable prepolymer, we selected polyester-polycarbonate copolymers as follows. Aliphatic polyesters, which are solid by nature, have been known to be biodegradable and biocompatible and have been used as a matrix or a scaffold in implant devices over the years.[9] On the other hand, aliphatic polycarbonates are quite a new family of biomaterials. Literature reports concerning the homopolymers of the six-membered cyclic carbonates, 1,3-dioxane-2-one or cyclic trimethylene carbonate derivatives show that they are few in number.[10] Poly(TMC) was prepared by ring-opening polymerization initiated with various transesterification catalysts including metal-alkoxides or -carboxylates. The glass transition temperature (T_g) of poly(TMC) was reported to be −38 to −17 °C, depending on the molecular weight.[10b] Low molecular weight polymers (MW < 6000) are oily, viscous liquids, whereas polymers with molecular weights between 6000 and 50 000 are soft, and sticky plastic, and those with molecular weights over 50 000 are harder but elastic rubbery materials. On the other hand, poly(CL) is crystalline with the melting point (T_m) of 63 °C and low T_g (−60 °C). The equimolar composition of high molecular weight copolymers of CL and TMC gave a T_g of around −48 °C and T_m close to room temperature, which were extrapolated from reported experimental values.[11] Relatively low molecular weight copolymers prepared in this study were viscous liquids, regardless of molecular weight (2500−12 000) and functionality.

In this study, we prepared coumarinated liquid biodegradable copolymers composed of CL and TMC repeating units on an equimolar basis. Multifunctionality of the copolymers was achieved by the use of multifunctional alcohol as an initiator. Irrespective of the type of alcohol used as the initiator, molecular weights of copolymers increased with the ratio of monomer to the number of hydroxyl groups (Figure 2). In general, photocuring depends on two factors: the molecular parameters of the photoreactive copolymer, which include its chemical structure, molecular weight, type of photodimerizable group, and functionality, and the operational conditions including the light source (wavelength), intensity of light, film thickness, and irradiation time. The dependence of the photocuring on molecular parameters and operational parameter showed that improved photocuring characteristics were observed for tetrabranched photoreactive copolymers in comparison to tribranched ones. This is due to the higher probability of intermolecular association of the coumarin groups and concomitantly easier formation of a network of cross-links, resulting in improved photocuring characteristics. Among photoreactive copolymers with the same functionality, there was little significant difference in photocuring characteristics (Figure 5), regardless of the molecular weight. This may be accounted for as follows. Higher molecular weight copolymers contain fewer photoreactive centers in their bulk as compared with their lower molecular weight counterparts. Therefore, a higher cross-linking rate is favored for lower molecular weight copolymers in terms of occurrence of photodimerization. However, an increase in molecular weight upon photodimerization is favored for higher molecular weight copolymers. These counteracting effects appear to level off or minimize the

effect of molecular weight of copolymer on photocuring characteristics at the same functionality.

As for the dependence of operation parameters, photocuring was facilitated in thinner films as expected (Figure 6). The initial photocuring rate increased proportionally to photointensity (Figure 8). The photocuring rate per photoenergy at a film thickness of 0.03 mm, which was calculated from the slope of the photocuring yield-intensity relationship, was 4.0 nm s^{-1}/mW cm^{-2} or 4.0 nm/mJ cm^{-2}. This means that at the photointensity of 100 mW/cm^2, photocuring proceeds at the rate of 24 μm/min in this particular application. The formation of multiple surface layers, on a fully coumarinated surface by a stereolithographic technique, was due to photodimerization of coumarin groups at layer/layer and at layer/substrate interfaces as well as within the layer (Figure 9).

In conclusion, we prepared a molecular design for the development of photocurable liquid biodegradable copolymers. These materials offer promising potential for application in biomedical fields including manufacture of microfabricated devices and surface layering. In vitro hydrolysis and in vivo performance of photocured copolymers and more detailed microarchitectured surfaces will be reported soon.

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