Poly(carbonate−acetal)s from the Dimer Form of Dihydroxyacetone

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ABSTRACT: The design and synthesis of new biomaterials, particularly those derived from biomolecule-based monomers, remains an area of considerable research effort. Herein the synthesis and characterization of poly(carbonate-acetal)s based on stabilized dimer forms of the glucolytic metabolite, dihydroxyacetone, are reported. The polymers possess glass transition (>40 °C) and thermal decomposition (>300 °C) temperatures exceeding those typically associated with aliphatic polycarbonates. The surface free energies of the polymers are significantly influenced by slight substitutions on the DHA dimer, and the polymer thin films support cell growth in culture.

Introduction

Polymeric biomaterials are often derived from biomolecular building blocks that are eliminated from the body through natural metabolic pathways. Successful examples include the polyesters poly(lactic-*co*-glycolic)-acid and poly(ϵ-caprolactone). These and other materials form the foundation for a number of biomedical devices that range from simple biodegradable sutures to complex drug delivery systems and engineered tissues.[1−4] Driven by the success of these biomaterials, there is a continued interest in the synthesis of new biomaterials to support increasingly sophisticated biomedical devices.[5−7]

Dihydroxyacetone (DHA) (**I**, Scheme 1) is an intermediate of glucose metabolism and is accepted by the FDA as the active ingredient in sunless tanning lotions.[8−10] These characteristics make it a potentially attractive building block for new polymeric biomaterials. However, in solution, monomeric DHA is in equilibrium with a hemiacetal dimer (**II**, Scheme 1), which complicates the chemistry for synthesizing well-defined polymers. In this paper, we report a strategy to synthesize DHA-based polymers with a locked form of the DHA dimer. The dimer was stabilized through substitution of an ethyl or isopropyl group at the tertiary alcohol at positions 2 and 5, and polymers derived from the stabilized dimer were synthesized by treatment with triphosgene (Scheme 1). The materials were chemically characterized using ^{1}H NMR, ^{13}C NMR, and elemental analysis, and their molecular weights were determined relative to polystyrene standards in THF by gel permeation chromatography. Thermal analysis by differential scanning calorimetry and thermogravimetric analysis showed the polymers had unexpectedly elevated T_g's (ranging between ∼40 and ∼60 °C) and decomposition temperatures (>300 °C). In addition to chemical and thermal characterization, the surface characteristics of spin-cast thin films were determined by contact angle goniometry from which their surface energies were calculated. The starting monomers were nontoxic to the HeLa cell line (up to 1 mg/mL), and thin films of the polymers supported cell growth as determined by in vitro culture with the NIH/3T3 cell line.

Experimental Section

Materials and Equipment. Dihydroxyacetone dimer (DHA), triethyl orthoformate, triisopropyl orthoformate, pyridine, and triphosgene were purchased from Aldrich and used as received. NMR spectra were recorded on Mercury 300 MHz, Inova 400 MHz, and Inova 500 MHz spectrometers. Gel permeation chromatography was carried out in a tetrahydrofuran (THF) mobile phase (1 mL/min) with UV (Waters 486) and RI (Waters 2410) detection. All molecular weights are relative to polystyrene standards. Thermal analyses were performed with either a TA Instruments Q1000 calorimeter with a heating/cooling rate of 10 °C/min and nitrogen flow rate of 50 mL/min or a TA Instruments Q500 thermogravimetric analyzer with a heating rate of 10 °C/min and nitrogen flow rate of 50 mL/min. Uniaxial compression experiments were conducted on an Instron instrument with a crosshead speed of 0.02 in./min at 20 °C and 50% humidity. The NIH/3T3 and HeLa cell lines were purchased from the American Type Culture Collection (Manassas, VA).

Synthesis of (2,5-Diethoxy-1,4-dioxane-2,5-dimethanol) (IIIa). Compound **IIIa** was synthesized using modifications of previously reported methods.[11−13] Dihydroxyacetone dimer (32 g, 177.8 mmol), triethyl orthoformate (60 mL, 360 mmol), and *p*-toluenesulfonic acid (*p*-TsOH) (128 mg) were combined in 300 mL of ethyl alcohol and stirred for 24 h, after which time 400 mg of Na_2CO_3 was added, and the reaction mixture was stirred for an additional 30 min and filtered. Removal of the solvent and residual triethyl orthoformate in vacuo and recrystallization of the product from ethyl acetate resulted in the title compound (31 g, 74%). ^{1}H NMR ($CDCl_3$) δ: 1.14−1.24 (6H), 3.4−3.9 (12H). Anal. Calcd: C, 50.85; H, 8.47. Found: C, 50.89; H, 8.69.

Synthesis of (2,5-Diisopropoxy-1,4-dioxane-2,5-dimethanol) (IIIb). Compound **IIIb** was synthesized in the same manner used for **IIIa** but substituting triisopropyl orthoformate in 2-propanol for the triethyl orthoformate in ethanol (yield 9.5%). ^{1}H NMR ($CDCl_3$) δ: 1.18−1.26 (12H); 3.4−4.2 (10H). Anal. Calcd: C, 54.53; H, 9.15. Found: C, 54.45; H, 9.06.

General Polycondensation Protocol. The following protocol was used to synthesize 1 g of polymer **IV.a.1** (Table 1). The same protocol was used to synthesize all reported polymers. Alterations to the protocol (temperature, time) and the effect on molecular weight are outlined in Table 1. To a solution of **IIIa** (1 g, 4.24 mmol) in pyridine (1.3 mL, 15.89 mmol) and 5 mL of dichloromethane at 30 °C was added dropwise a solution of triphosgene (0.53 g, 1.78 mmol) in 1 mL of dichloromethane over 45 min. After complete addition, the mixture was allowed to stir for an additional 5 min,

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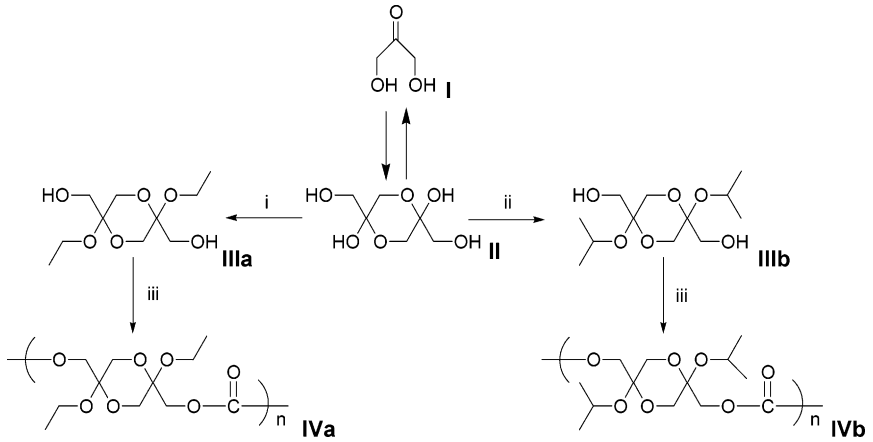
Scheme 1. Synthetic Route for Poly(carbonate−acetal)s Based on a Locked Dimer of Dihydroxyacetone[a]



[a] Reagents and conditions: (i) triethyl orthoformate, EtOH, *p*-TsOH (cat.), RT; (ii) triisopropyl orthoformate, 2-propanol, *p*-TsOH (cat.), RT; (iii) triphosgene, pyridine, CH_2Cl_2.

Table 1. Polymerization Reaction Conditions, Product Yield, Weight-Average Molecular Weight, Polydispersity (M_w/M_n), and Glass Transition Temperature for Poly(carbonate−acetal)s Based on Monomers IIIa and IIIb

sample	stabilizing group	temp; time conditions	yield, %	$M_w \times 10^{-3}$	M_w/M_n	T_g, °C
IVa.1	ethyl	30 °C; 45 min	87	48.4	2.0	61
IVa.2	ethyl	15 °C; 45 min	76	42.7	2.2	54
IVa.3	ethyl	0 °C; 45 min	68	28.0	1.9	42
IVa.4	ethyl	15 °C; 15 min	56	36.7	2.1	47
IVb.1	isopropyl	30 °C; 45 min	93	43.7	1.7	54

followed by direct precipitation into methanol. The resulting white solid was collected by filtration, washed with methanol, and dried to constant weight under vacuum. Characterization of **IVa.1** (ethoxy substitution): ^{1}H NMR ($CDCl_3$) δ: 1.10−1.25 (6H), 3.40−3.90 (8H), 4.0−4.4 (4H). ^{13}C NMR ($CDCl_3$) δ: 155 (−O−*C*O−O−), 94−98 (apical C), 64−67 (acetal carbons), 57 (−*C*H_2−CH_3), 15 (−*C*H_3). Anal. Calcd: C, 50.38; H, 6.92. Found: C, 50.29; H, 6.94. Characterization of **IVb.1** (isopropoxy substitution): ^{1}H NMR ($CDCl_3$) δ: 1.1−1.3 (12H), 3.5−4.3 (10H). ^{13}C NMR ($CDCl_3$) δ: 155 (−O−*C*O−O−), 95−98 (apical C), 62−65 (acetal carbons), 57−66 (−*C*H_2−CH_3), 24 (−*C*H_3). Anal. Calcd: C, 53.78; H, 7.64. Found: C, 53.66; H, 7.62. Molecular weights are reported in Table 1.

Contact Angle Measurements. Contact angle goniometry was performed under ambient conditions with a Ram6-Hart telescopic goniometer with a Gilmont syringe equipped with a 24 gauge flat-tipped needle. The probe fluids used were water (Milli-Q, 10^{18} Ω/cm) and diiodomethane purified by vacuum distillation. Dynamic advancing (θ_A) and receding contact angles (θ_R) were recorded while the probe fluid was added to and withdrawn from the drop, respectively. Contact angles were measured on polymer thin films obtained by spin-coating on silicon wafers with solutions of polymer in THF (100 mg/mL; 200 μL per wafer).

Cell Culture. The NIH/3T3 and HeLa cell lines were maintained in phenol red-free Dulbecco's Modified Eagle Medium with 4 mM L-glutamine, 10% (v/v) calf serum, penicillin (100 units/mL), and streptomycin (100 μg/mL). Cultures were maintained at 37 °C in a humidified 5% CO_2 atmosphere and were split by trypsinization.

Cell Attachment and Growth. Thin films of polymers **IVa.1** and **IVb.1** were spin-cast from THF solution onto sterilized glass coverslips. The coverslips were added to six-well plates and immediately covered with NIH/3T3 cells in growth media at a concentration of 5000 cells/mL. Cells were allowed to attach and grow over 72 h under normal cell growth conditions (above).

In Vitro Cytotoxicity Measurement. HeLa cells were grown in clear, flat-bottom tissue culture polystyrene 96-well plates (Costar) at an initial density of 5000 cells per well in 200 μL of growth medium. After 24 h, the growth medium was removed and replaced with a mixture containing 110 μL of growth medium and 40 μL of polymer dissolved in Dulbecco's phosphate buffered saline. Final polymer concentrations in the medium ranged from 0 to 1 mg/mL. The cells were incubated for 4 h, after which the polymer-containing medium was removed and replaced with 105 μL of growth medium. Following an additional 48 h of incubation, 20 μL of CellTiter 96 Aqueous One Solution Cell Proliferation Assay (MTS) reagent (Promega) was added to each well. The samples were incubated for an additional 1 h at 37 °C, and the absorbance at 490 nm of each well was read in a microplate spectrofluorometer (SpectraMax, Molecular Devices, Sunnyvale, CA). Growth was normalized to the untreated cell population.

Results and Discussion

Scheme 1 shows the complete synthetic route to the DHA-dimer polycarbonates. Because the utility of a biomaterial can be expense-limited by an excessive number of synthetic steps, we set out to design a straightforward and high yielding synthetic route to make the final polymer using the fewest number of synthetic steps.

The dimer form of DHA was previously synthesized for studies in sugar chemistry and basic spectroscopic studies.[11−13] To our knowledge, only the diethoxy form of the dimer (**IIIa**) has been reported. To investigate the influence of substitutions at the 3° alcohol upon the polymer properties, we synthesized an additional DHA analogue containing an isopropyl substituent. The diethoxy-substituted DHA dimer (**IIIa**) was synthesized in one step by treating an ethanolic suspension of DHA with triethyl orthoformate in the presence of a catalytic amount of *p*-TsOH. The isopropoxy-substituted DHA dimer (**IIIb**) was synthesized through adaptation of same protocol. A fortunate attribute of these compounds is that they were both isolated by recrystallization and are solids at room temperature, making them easy to purify and handle. The carbon and hydrogen results from the elemental analysis of both **IIIa** and **IIIb** are consistent with their theoretical contents. It is important to note that these stabilized forms of the DHA dimer can exist in either the cis- or trans-isomer form.[13]

Because these isomeric species were not isolated individually, the ^{1}H NMR signals are more properly defined as regions rather than exact chemical shifts.

The free hydroxyl groups on **IIIa** and **IIIb** are attractive for the synthesis of a number of polymer types including polycarbonates, polyesters, and polyurethanes. The unsubstituted DHA dimer (**II**) contains two hemiacetals in its six-membered ring that are converted to the more stable acetal group upon the formation of **IIIa** and **IIIb**. Because the acetal group retains its own unique characteristics, most notably hydrolytic instability at acidic pH, polymers based on **IIIa** and **IIIb** are best categorized as belonging to the polymer class denoted poly(*XXXX*-acetal), where *XXXX* reflects the linkage between the DHA dimer hydroxyl groups. The combination of polymer linkers, particularly for biomaterials (i.e., poly(carbonate−esters), etc.), is a common strategy to create polymers with chemical and physical characteristics that differ from their respective homopolymers.[14−16] The use of the acetal functional group in polymer-based drug delivery systems has been recently reported, primarily to impart pH sensitivity to the material.[17−20]

In this initial report, we focused on the synthesis and characterization of polycarbonates, or poly(carbonate−acetal)s, based on **IIIa** and **IIIb**. Polycarbonates and combination polymers containing the carbonate linkage are intriguing candidates for high-strength applications in tissue engineering,[21,22] matrices for controlled drug delivery,[23−25] and patterned surfaces for cell growth.[26]

Polymers **IVa** and **IVb**, derived from monomers **IIIa** and **IIIb**, respectively, were synthesized by solution polycondensation. To minimize the potential health and safety issues associated with phosgene-based polycondensation, the solid phosgene analogue, triphosgene, was substituted with favorable results. For each polymer, purification was afforded by direct precipitation of the reaction into methanol. Polycarbonates are typically synthesized using an excess of the carbonyl donor (i.e., triphosgene), which complicates the control over final molecular weight by stoichiometric reagent variation. Therefore, to gain control over the desired molecular weight, the reaction temperature and the rate of triphogene addition were used as variable parameters. By varying temperature and rate of triphosgene addition, polymers with M_w ranging from ∼28 000 to ∼48 000 Da were synthesized with good yield (Table 1). These molecular weights are consistent with other prominent polymeric materials used for biomedical applications, particularly poly(lactic-*co*-glycolic acid) polyesters, although further increasing the molecular weights of these new materials could lead to enhanced mechanical properties with wider biomedical applications.

Holding the triphosgene addition time constant and varying the temperature (samples **IVa.1**, **IVa.2**, and **IVa.3**) led to incrementally lower molecular weights as the temperature was decreased. For the polycondensation of **IIIa** by treatment with triphosgene over 45 min, the M_w relates to the reaction temperature (T given in °C) by the second-order fit equation $M_w = -0.02T^2 + 1.28T + 28$ ($r^2 = 1.0$), whereas the M_n relates to the reaction temperature by the linear equation $M_n = 0.03667T + 13.833$ ($r^2 = 0.9997$). These relationships can allow the a priori determination of a desired M_w or M_n (at least between M_w ∼28K and ∼48K) by altering the temperature of reaction; however, the second-order M_w fit suggests that extrapolations significantly beyond

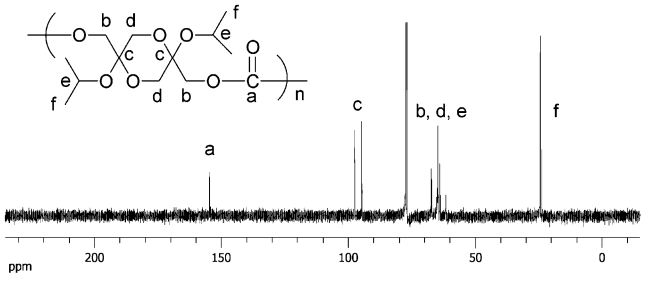


Figure 1. ^{13}C NMR spectra of polymer **IVb.1** and corresponding peak assignments.

30 °C may not lead to significantly greater M_w, likely because the increased temperature cannot compensate for the exponential decline in available reactive monomer ends. Holding temperature constant and increasing the rate of triphosgene addition (comparing samples **IVa.2** and **IVa.4**) led to comparable molecular weights, but with lower yield with the more rapid addition rate. Altering the substitutent at positions 2 and 5 (i.e, diethoxy vs isopropoxy) does not appear to strongly influence polymerization since samples **IVa.1** and **IVb.1** (30 °C; 45 min addition rate for each polymerization) have comparable M_w and yield.

The chemical composition and structure of all polymers were characterized by elemental analysis, ^{1}H NMR, and ^{13}C NMR. The elemental analysis for all polymers was within 0.2% of the theoretical carbon/hydrogen contents. The purity of the final products is unexpectedly high since it was achieved by direct precipitation of the reaction mixture. As previously mentioned, the monomers **IIIa** and **IIIb** consist of isomers that were not isolated individually. Therefore, the peak assignments provided in the ^{1}H NMR are ranges rather than individual peaks. A representative ^{13}C NMR spectrum and chemical shift peak assignments are shown in Figure 1 for polymer **IVb.1** (equivalent results were obtained for polymers **IVa.1**−**IVa.4**). Polymers from both monomers are soluble in chlorinated organic solvents and THF and are insoluble in aliphatic alcohols and water.

Thermal characterization by differential scanning calorimetry showed a single glass transition temperature (T_g) for each polymer. The T_g's (Table 1) were considerably higher than typically observed for aliphatic polycarbonates such as poly(ethylene carbonate) (T_g 5−20 °C)[23] and poly(1,3-trimethylene carbonate) (T_g −15 °C).[27] In comparison, the more common polycarbonates based on the aromatic bisphenol A monomer have T_g's in the ∼150 °C range[28] and aromatic polycarbonate biomaterials based on tyrosine have T_g's between ∼50 and 90 °C, depending upon the particular structure.[29] Presumably the ring structure of monomers **IIIa** and **IIIb** imparts a degree of chain rigidity, leading to a higher than expected T_g for an aliphatic polycarbonate, but not equivalent to the rigidity observed for aromatic polycarbonates. The T_g of **IVa** depends on molecular weight. The dependence of T_g upon M_n is shown in Figure 2 and correlates to the relationship

$$T_g = T_g^{\infty} - \frac{K}{M_n} \quad (1)$$

where T_g^{∞} is the glass transition temperature at infinite M_n and K is a constant specific for the polymer under consideration.[39] From this relationship, the es-

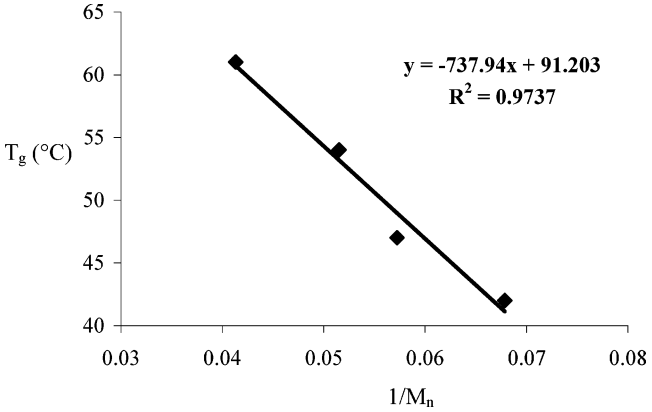


Figure 2. Dependence of T_g on M_n. Extrapolation to infinite M_n reveals a calculated T_g of ~91 °C.

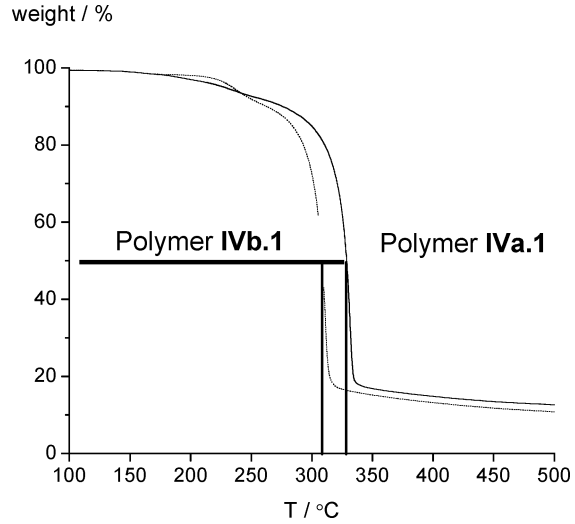


Figure 3. TGA profile showing the 50% decomposition temperature for polymers **IVa.1** (T_{d50} = 328 °C) and **IVb.1** (T_{d50} = 308 °C).

timated T_g^∞ for polymer **IVa.1** (given as the *y*-intercept in Figure 2) is ~90 °C. The polymers appear to be amorphous since no T_m was observed in all DSC traces, although this is an issue that will require more detailed investigation since the extent of polymer crystallinity is a function of the polymer isolation and fabrication methods. Somewhat surprisingly, however, the thermal stability of the DHA-dimer polymers approaches that of the aromatic polycarbonates. Figure 3 shows the thermal decomposition profile for polymers **IVa.1** and **IVb.1**. The point at which 50% of the polymer decomposes (denoted as T_{d50}) for both polymers exceeds 300 °C, which is consistent with the T_d's reported for the tyrosine-based polycarbonates.[29]

The mechanical characteristics of these DHA-based polymers are also intriguing. Cylindrical pellets of polymer samples **IVa.1** and **IVb.1** were formed (100 mg samples, aspect ratio = 0.5) and then subjected to unconfined uniaxial compression to create stress vs strain profiles. The results (similar for both polymer samples, data not shown) revealed a Young's compression modulus of 0.8 ± 0.01 GPa and a compressive yield strength of 45 ± 5 MPa. From the perspective of a biomaterial, these values suggest that these poly(carbonate−acetal)s may be useful in high-strength tissue engineering applications since their compression characteristics are closely comparable to cancellous bone with similar dimensions.[30,31]

Table 2. Advancing and Receding Contact Angles and Calculated Free Surface Energies of Polymers IVa.1 and IVb.1

	contact angle θ, deg				
polymer	H_2O (adv/rec)	CH_2I_2 (adv/rec)	γ^d, mJ/m^2	γ^p, mJ/m^2	γ_s, mJ/m^2
IVa.1	76 ± 1/60 ± 2	44 ± 1/19 ± 2	33.8	6.3	40.1
IVb.1	88 ± 2/72 ± 1	56 ± 1/32 ± 2	28.7	3.1	31.8

These data prompted investigation of the polymer surface properties because the interfacial characteristics of a biomaterial strongly influence its interaction with surrounding cells and tissue.[32,33] To determine the surface properties of spin-cast films of polymers **IVa.1** and **IVb.1**, advancing and receding contact angles were measured. The contact angle results, organized in Table 2, show that both polymers have relatively hydrophobic surfaces that are comparable to those reported in the literature for the polyesters based on lactic and glycolic acid.[34] The difference between the advancing and receding contact angles, defined as contact angle hysteresis, speaks to the heterogeneity of the surface, its roughness, the degree to which the liquid permeates the surface, and/or the extent to which the material surface reconstructs in response to the drop.[35] The hysteresis observed for polymers **IVa.1** and **IVb.1** is relatively small, suggesting that the spin-cast polymers were smooth and that the water droplet did not significantly alter the surface properties of the polymer. These results are not surprising since the polymers are hydrophobic, and the experiments were performed at room temperature, well below the T_g of the polymers.[36] The advancing and receding contact angles for these two polymers indicate that the surface of polymer **IVb.1** is more hydrophobic than **IVa.1**, consistent with the more hydrophobic isopropyl group in polymer **IVb.1**.

To derive the surface free energy (γ) of these polymers, the method developed by Owens and Wendt[37] was applied, where by the free energy of a surface is given as the sum of the dispersive and the polar components (eq 2).

$$\gamma_i = \gamma_i^d + \gamma_i^p \tag{2}$$

By measuring the contact angle between the polymer surface and two pure liquids with known dispersive and polar components, most commonly water (γ^d = 22.1 mJ/m^2; γ^p = 50.7 mJ/m^2) and diiodomethane (CH_2I_2: γ^d = 49.5 mJ/m^2; γ^p = 1.3 mJ/m^2) (see Table 2), the free surface energy of the material can be calculated from a system of two equations, i.e., eq 3 used twice (once for each liquid, in this case water and diiodomethane) where γ_L is the overall surface tension of the liquid, γ_L^d and γ_L^p are its respective dispersive and polar contributions, and γ_S^d and γ_S^p are the respective dispersive and polar contributions to the solid surface energy.

$$(1 + \cos\Theta)\gamma_L = 2\{(\gamma_L^d\gamma_S^d)^{1/2} + (\gamma_L^p\gamma_S^p)^{1/2}\} \tag{3}$$

The free surface energy values calculated for polymers **IVa.1** and **IVb.1** (Table 2) show that substitution of an isopropyl (polymer **IVb.1**) for an ethyl group (polymer **IVa.1**) decreases the surface energy by ~8 mJ/m^2.

The surface energies of these two polymers straddle the surface energy of polyesters based on lactic and glycolic acid (~35 mJ/m^2).[34] Interestingly, the surface energies of PLGA polymers are not significantly altered

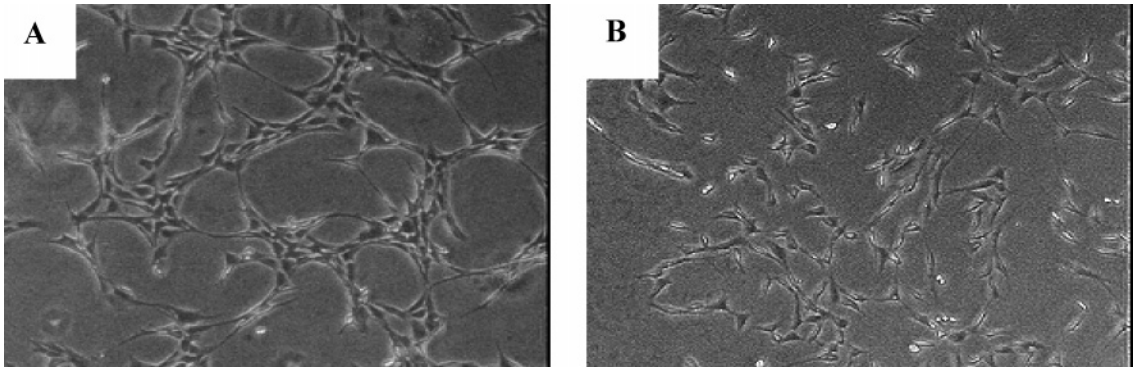


Figure 4. NIH/3T3 cell growth pattern 72 h postseeding onto thin films of polymers **IVa.1** (A) and **IVb.1** (B).

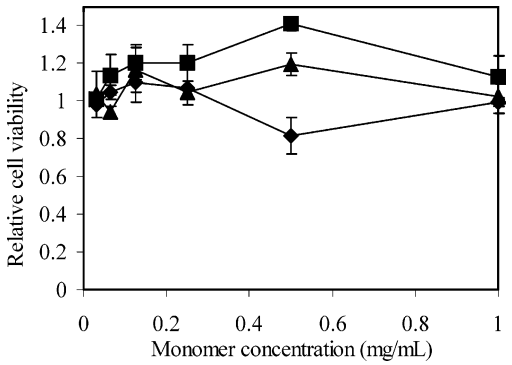


Figure 5. Cell viability as a function of DHA (closed diamond), **IIIa** (closed squares), and **IIIb** (closed triangle) concentration (mg/mL) ($n = 3$).

by the addition/subtraction of a single methyl group (corresponding to the lactic acid/glycolic acid ratios), presumably due to preferred chain orientation at the solid/air interface during solvent spin-casting. However, for polymers **IVa.1** and **IVb.1** the addition/subtraction of a single methyl group (the only structural difference between polymers **IVa.1** and **IVb.1**) has a significant effect, which suggests that the surface energies may be tunable by alteration of the substitutent at the 2,5-position or by copolymerization of monomers **IIIa** and **IIIb**.

As an initial evaluation of whether these materials can support cell growth, the polymers were spin-cast from solution onto glass coverslips, seeded with the NIH/3T3 cell line (5000/mL) and observed over 72 h. The cells quickly attached to both polymer surfaces and remained spread (i.e., in their characteristic growth morphology) on the polymer surface through 72 h postseed (Figure 4). Viability of the cells at 72 h was >99% as measured by trypan blue exclusion (data not shown). Like other water-insoluble polymeric biomaterials, the hydrophobicity of the polymer surfaces likely leads to nonspecific absorption of serum proteins to create an interface that is favorable to cell growth. This phenomenon has inspired strong research efforts that focus on chemical and physical surface modification of biomaterials to optimize the interaction at the material/cell interface.[38] Additionally, the cytotoxicity of both protected dimers (**IIIa** and **IIIb**) was evaluated as a function of concentration by measuring cellular metabolic activity with the MTS assay (a modified form of the MTT assay) (Figure 5). The results indicate that both dimers do not disrupt metabolism relative to untreated cells, even up to 1 mg/mL. While these initial cytotoxicity results are promising, the complete composition of degradation products for polymers **IVa** and **IVb** are yet unknown and a full biocompatibility evaluation is still necessary to determine whether these new materials will be useful as biomaterials.

Conclusions

In this report, the synthesis, chemical characterization, and physical characterization of two poly(carbonate-acetal)s based on two forms of a stabilized dihydroxyacetone dimer are described. The polymers differed by one methyl group at positions 2 and 5. Weight-average molecular weights approaching 50 000 were obtained by solution polycondensation with triphosgene, with polydispersities of ~2.0. The T_g's and thermal decomposition temperatures of the polymers were higher than expected when compared to those of other aliphatic polycarbonates. The surface energies of the polymers differed considerably with the addition of a single methyl group ($\Delta \sim 8$ mJ/m^2), in contrast to the small difference in surface energies observed for polyesters based on lactic and glycolic acid, which also differ by a single methyl group. The polymers supported cell attachment and growth over 3 days in culture, and both protected DHA dimers did not disrupt cell growth at the highest concentration tested (1 mg/mL).

These results point to a number of interesting fundamental and applied considerations that will be a continued focus of research in our laboratory, such as the rates and mechanisms of hydrolytically/enzymatically catalyzed polymer degradation, the characteristics of polymers (and copolymers) synthesized from isolated cis/trans conformations, in vivo biocompatibility, and the ability of these polymers to control the rate of drug release into the body.

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