

Biodegradable and Tunable Poly(carbonate-ester)s Based on Units of ϵ -caprolactone and Glycerol

Jesse Wolinsky and Mark W. Grinstaff

Boston University Department of Biomedical Engineering Boston, MA 02215

Statement of Purpose: Biodegradable polymers offer significant advantages over permanently implanted materials,¹⁻³ but are distinctly limited by the range of properties attainable and lack of chemical side groups for further functionalization, thus potentially hindering the development and synthesis of more advanced and tailored materials for biomedical applications.⁴ We have synthesized and characterized a series of novel degradable carbonate-based polymers that feature alcohol, amine, or carboxylic acid functionalization for the purpose of further modification towards enhancement of polymer properties and/or conjugation with biologically-relevant compounds such as therapeutic agents or dyes.

Methods: A series of biodegradable copolymers comprised of ϵ -caprolactone and glycerol-based monomer units were synthesized using varying monomer ratios and stannous 2-ethylhexanoate as the catalyst, as shown in Figure 1.

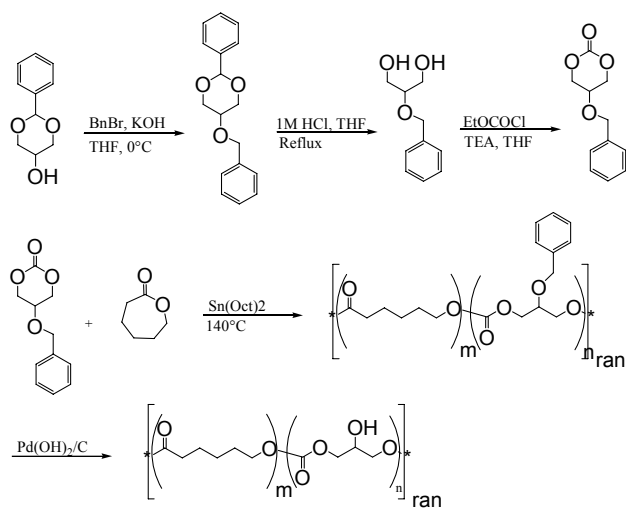


Figure 1. Copolymer synthesis via ring-opening polymerization.

A representative copolymer was further functionalized with 6-benzyloxy-hexanoic acid, hexanedioic acid monobenzyl ester, or Fmoc-6-amino-hexanoic acid and subsequently deprotected to yield an alcohol, carboxylic acid, or amine-derivatized polymer, respectively. Copolymer sequence and structure were characterized via nuclear magnetic resonance (NMR), molecular weights and polydispersity by size exclusion chromatography (SEC), and thermal transitions with differential scanning calorimetry (DSC). To demonstrate the utility of modifiable biomaterials, fluorescent nanoparticles were prepared by reacting amine-derivatized copolymer to fluorescein isothiocyanate (FITC) dye molecules, processed via an emulsion/solvent evaporation method, and sized using dynamic light scattering (DLS).

Results/Discussion:

ϵ -caprolactone has been polymerized with the glycerol-based monomer 5-benzyloxy-1,3-dioxan-2-one to afford a series of poly(ester-carbonates) containing monomer mole ratios ranging from 0% to 100% glycerol content. Relative mole fractions of monomers in the copolymer were determined by ¹H NMR. Molecular weights range from 3,000 to 23,000 g/mol depending on monomer ratio as measured by size exclusion chromatography. Thermal analysis via differential scanning calorimetry (DSC) showed the glass transition temperature of the copolymers increasing from -64°C to -10°C with increasing glycerol content, while the melting temperature decreases from 57°C to 22°C before disappearing altogether above 20% glycerol mole ratio, indicating a lack of crystallinity beyond this composition. A representative copolymer was further functionalized with a series of common reactive groups, including an alcohol, amine, or carboxylic acid, to afford a series of biodegradable copolymers capable of subsequent modifications with a large variety of chemistries. Nanoparticles, approximately 200 nm in mean diameter as measured by dynamic light scattering, were prepared using a FITC-modified amine-derivatized copolymer for potential imaging and drug delivery applications.

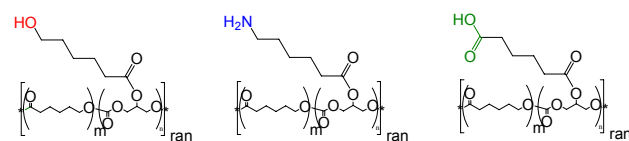


Figure 2. Copolymers functionalized with alcohol, amine, or carboxylic acid side groups.

Conclusions: Synthesis of novel poly(ester-carbonates) derived from glycerol and 6-hydroxycaproic acid repeating units was achieved by ring-opening polymerization followed by subsequent catalytic hydrogenolysis, yielding a series of biodegradable copolymers featuring reactive secondary alcohol side groups. These groups were further reacted to afford primary alcohol, amine, and carboxylic acid derivatives, further demonstrating that chemical, physical, and mechanical properties can be tailored by varying copolymer units, composition, and side group moieties. Synthesis of new polymers designed for specific drug delivery, medical device, and tissue engineering applications will be facilitated by the synthesis of such novel biodegradable and tunable materials.

References:

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