Synthesis of biodegradable polymers by enzymatic ring-opening polymerization of ε-caprolactone and isosorbide

M.D.J. Ramírez-Quijas, Karla A. Barrera-Rivera and Antonio Martínez-Richa*
Facultad de Química, Universidad de Guanajuato, Noria Alta S/N, 36050, Guanajuato, Gto., México
*richa@quijote.ugto.mx

1. Introduction

The ability to attach synthetic polymers onto carbohydrates is a pathway to new applications in the fields of detergents, packaging, and pharmaceuticals, and it increases the biodegradability of the target polymers. However, selective functionalization of carbohydrates is complicated, since carbohydrates contain multiple hydroxyl groups. Selective monoacylation of the carbohydrate is difficult without using protective group strategies. Deprotection is the required and the synthetic scheme becomes complex. Enzymes are highly selective and therefore they have been used to regioselectively acylate carbohydrates with lipase-catalyzed polyester synthesis, would be an attractive alternative to poorly selective chemical catalysts [1]. Water soluble and dispersible polymers are in great demand for applications as detergents and surfactants. Low molecular weight amphiphilic compounds such as fatty acid esters of carbohydrates also function as useful surfactants. Therefore, incorporation of sugars as components of aliphatic polyesters appears to be a promising strategy for the design of new amphiphilic structures [2]. Recently, enzyme-catalyzed reactions have been demonstrated to provide high selectivity for the acylation of various carbohydrates. Specifically, lipases and proteases have been successfully used for the acylation of the primary hydroxyl group(s) of sugars (glucose, lactose, maltose, etc.) in polar aprotic solvents [2].

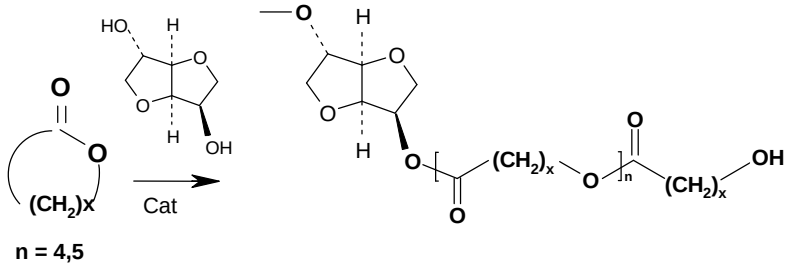
2. Experimental conditions

Lipase production by *Yarrowia lipolytica* was made as previously reported by Barrera *et al* [3]. Lewatit beads were purchased form Sigma-Aldrich. Before immobilization, resin was activated with ethanol and washed with distilled water. Enzyme immobilization was carried out according to the procedure reported by Sandoval *et al* [4]. The immobilized enzyme preparations were dried under vacuum for 24 h at room temperature. Isosorbide

(Aldrich) was recrystallized twice from dry acetone, DL-lactide (Aldrich) was used as received. Prior to its use Isosorbide and DL-Lactide were dried over P_2O_5 in a desiccator for 24 h at room temperature. ε-CL (Aldrich) was distilled at 97-98 °C over CaH_2 at 10 mmHg. Two types of polyesters were synthesized in bulk by ring-opening polymerization. Synthesis of PCL-Isosorbide and PLA-Isosorbide: (1 mmol ε-CL: 1 mmol Isosorbide, 1 mmol DL-Lactide: 1 mmol Isosorbide) and 12 mg of immobilized lipase were added to 10 mL vial, sealed, and kept in an oil bath at predetermined temperature and time. Conversions were monitored by ^{1}H-NMR. Products were purified by dissolving in chloroform (1 volume), precipitating in methanol (10 volume), and drying in a desiccator at room temperature.

3. Results and discussion

Isosorbide was used as the multifunctional initiator for ε-caprolactone (*ε*-CL) and DL-Lactide ring-opening polymerizations (Scheme 1). This provided a novel route for the one-pot synthesis of oligomers with isosorbide headgroups.



Scheme 1. *Yarrowia lipolytica catalyzed polymerization of lactones and isosorbide to form biodegradable amphiphilic polyesters.*

Figure 1 shows the kinetic studies in function of time and isosorbide concentration. Lowest conversions of ε-CL to PCL-isosorbide were observed when lipase was immobilized on Lewatit 1065. One of the reasons of this behavior is the distribution of the enzyme into the polymeric resin, which is affecting the specificity of the enzyme. In the PLA-Isorsorbide synthesis, the ^{13}C NMR spectra obtained for the product in the expanded region of the carbonyl grouping displayed additional peaks, which could emerge from the interactions of the different moiety sequences random distributed along the cooligomer chains. The relative great number of extra peaks also indicates that undesirable intermolecular transisterification reactions may have occurred and suggesting that block cooligomers were obtained and

secondary intermolecular transesterification reactions occurred and, hence, shorter blocks are expected as result.

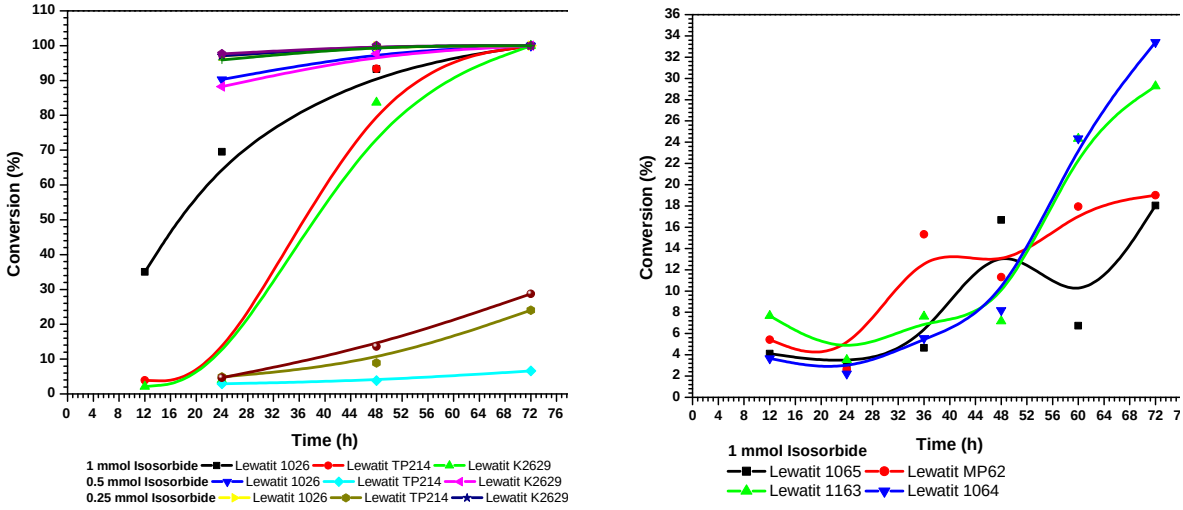


Figure 1. *Monomer conversion as a function of time for the enzyme-catalyzed ε-caprolactone-isosorbide polymerizations at 70 ℃. R= 1 mmol ε-CL/12 mg immobilized lipase. Effect of immobilization matrix and isosorbide concentration.*

4. Conclusions

A convenient one-pot biocatalytic synthesis of novel biodegradable amphiphilic oligomers is described. The selectivity of different immobilization matrices and general applicability of the method was also demonstrated by screening a number of commercial matrices with *Yarrowia lipolytica* lipase. Thus, by this strategy, chains were formed having sugar headgroups without using protection-deprotection strategies.

References

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