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PII: S1385-8947(18)31741-8
DOI: https://doi.org/10.1016/j.cej.2018.09.033
Reference: CEJ 19872

To appear in: *Chemical Engineering Journal*

Received Date: 17 January 2018
Revised Date: 22 August 2018
Accepted Date: 6 September 2018

Please cite this article as: W. Huang, N. Zhu, Y. Liu, J. Wang, J. Zhong, Q. Sun, T. Sun, X. Hu, Z. Fang, K. Guo, A novel microfluidic enzyme-organocatalysis combination strategy for ring-opening copolymerizations of lactone, lactide and cyclic carbonate, *Chemical Engineering Journal* (2018), doi: https://doi.org/10.1016/j.cej.2018.09.033

A novel microfluidic enzyme-organocatalysis combination strategy for ring-opening copolymerizations of lactone, lactide and cyclic carbonate

Weijun Huang[a, c, d], Ning Zhu[a, c, d]*, Yihuan Liu[a, c, d], Jian Wang[a, c, d], Jun Zhong[a, c, d], Qin Sun[a, c, d], Tao Sun[a, c, d], Xin Hu[b, c, d], Zheng Fang[a, c, d] and Kai Guo[a, c, d]*

[a] College of Biotechnology and Pharmaceutical Engineering, [b] College of Materials Science and Engineering, [c] State Key Laboratory of Materials-Oriented Chemical Engineering, [d] Jiangsu National Synergetic Innovation Centre for Advance Materials, Nanjing Tech University, Nanjing 211800, China

ningzhu@njtech.edu.cn or guok@njtech.edu.cn

Abstract: A novel microreactor-based enzyme-organocatalysis combination strategy was developed for ring-opening copolymerizations of varied types of cyclic monomers. Commercial Novozyme 435 (N435) and 1,5,7-triazabicyclo [4.4.0] dec-5-ene (TBD) were chosen as the model enzyme and organocatalyst for evaluating the polymerizations of ε-caprolactone (CL), δ-valerolactone (VL), L-lactide (LLA) and trimethylene carbonate (TMC) in the batch and microreactor respectively. Due to the catalytic selectivity, enzymatic polymerization cannot yield block copolymers containing PLA segment and organocatalysis showed poor activity toward CL polymerization. To address these challenges, enzyme and organocatalysis was combined based on microflow technology. In the assembled tandem microreactor system, series of well-defined triblock copolymers, such as PCL-*b*-PTMC-*b*-PVL, PCL-*b*-PTMC-*b*-PLLA and PTMC-*b*-PCL-*b*-PLLA, were efficiently prepared in the flow mode. The convenience of handling the copolymerization conditions and processes, reduced overall reaction time, well-controlled molecular weights and distributions were achieved by employing this microfluidic enzyme-organocatalysis combination strategy.

Introduction

Well-defined aliphatic polyesters have attracted great attention due to their biodegradability and biocompatibility, which are suitable for biomedical applications [1-4]. Lactones, carbonates and lactides, are the three major types of cyclic monomers for synthesis of aliphatic polyesters. Through ring-opening polymerization (ROP) di-, tri- or multi- block copolymers could be prepared with the tunable properties and broad applications [5-7].

The ring-opening polymerization methodologies have been developed by using metal complex [8-11] enzyme [12-15] or organic molecule as the catalyst [16-19]. Metal-mediated polymerizations always obey “coordination-insertion” mechanism [8] and the enzymatic processes follow “activated monomer” route [13]. To meet the high demand for metal-free biomaterials, organocatalysis have been reported based on varied mechanisms, including “electrophilic monomer activation”, “nucleophilic monomer activation”, “initiator or chain-end activation” and “bifunctional activation of monomer and initiator/chain end” [16]. Although cyclic monomers exhibited similar polymerization activities, the catalytic selectivity still remained [20]. In other words, it is challenging to conduct ring-opening copolymerizations (ROCP) of all three types of monomers of lactone, lactide and cyclic carbonate by using single catalysis. Recently, catalyst switch strategy was presented to fabricate block copolymers [21-23].

Traditionally, polymerizations were conducted in the batch reactor (BR), e.g. the ampoule. These batchwise reactions suffered from the poor control of polymerization conditions and processes, long polymerization time and the batch-batch variety, etc [24]. Flow chemistry in the microreactor (MR) is an attractive way to improve the chemical transformations due to the exquisite control of reaction parameters, extremely rapid heat/mass transfer, and no back mixing, which offer great advantages over the traditional batch reactors [25-27].