**Lipase-Catalyzed Solvent-Free Production of (Meth)Acrylate Monomers.**

Wouter Van Hecke, Arjan Heeres, Yamini Satyawali, Karolien Vanbroekhoven

*VITO (Flemish Institute for Technological Research) Boeretang 200 2400 Mol (Belgium)*

*\*Corresponding author:* [*wouter.vanhecke@vito.be*](mailto:wouter.vanhecke@vito.be)

**Highlights**

* (meth)acrylate esters were obtained at industrially appealing titers;
* nonlinear regression technique was applied to determine reaction rate constants;
* statistical inference was applied to the parameter estimates;
* second order kinetic model fits well with experimental results;

Introduction

Specialty or sensitive (meth)acrylate monomers are most often not available in the desired purity and quantity. Therefore, a milder and more sustainable manufacturing process is highly sought after [1]. To this end, lipases are known to catalyze ester synthesis at moderate conditions. Several of these have already been used to catalyse the production of (meth)acrylate esters with different alcohols in the presence of an inert organic solvent [1-3]. However, downstream processing could be simplified in solventless conditions [4, 5]. Hence, the first objective of this study was the solventless lipase catalysed transesterification of (meth)acrylates with various (bio-based) alcohols, enabling a more sustainable process for the production of specialty monomers. The second objective of this manuscript is to develop a generic kinetic model allowing simulation of the entire course of the solventless conversion based on nonlinear regression techniques.

Methods

## Enzymes & chemicals

Novozym 435 (Novozymes, Bagsværd, Denmark) was used as catalyst in all tests. All organic alcohols and the methyl(meth)acrylate used for the transesterification had purities above 98% and were purchased from Sigma-Aldrich (Schnelldorf, Germany). A molecular sieve UOP Type 5Å (Sigma-Aldrich, Schnelldorf, Germany) was used to remove methanol.

## Reaction conditions & nonlinear regression procedures

The lightest boiling substrate is added in molar excess to allow close to complete conversion of the highest boiling substrate and to avoid excessive temperatures in the subsequent distillation tower. Therefore, the conversions were only studied in reaction regimes using a molar excess of methyl (meth)acrylate. More detailed information on reaction conditions and the applied nonlinear regression procedures can be found in Heeres et al. [6].

Results and **discussion**

The ping-pong reaction mechanism seems to be the preferred model to describe lipase kinetics. A good fit with high R2 values resulted from the selection of this mechanism. However, the large confidence intervals suggested overparameterization of the model. The use of a simpler second order rate equation yielded a more accurate model. Table 1 shows the results of the simulations. Higher reaction rate constants were systematically obtained for the transesterification of methyl acrylates, proving this to be a more accepted substrate than methyl methacrylate.

Table 1. The regressed second order reaction rate constants ranked in decreasing order. The lower and upper limit (LL and UL) of the 95% confidence intervals (CI) are also given.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Alcohol | Methyl ester | kcat  kg/(mol·h) | CI LL  kg/(mol·h) | CI UL  kg/(mol·h) |
| Tetrahydrofurfuryl alcohol | Methyl acrylate | 1.69 | 1.26 | 1.71 |
| Citronellol | Methyl acrylate | 1.31 | 1.18 | 1.45 |
| Furfuryl alcohol | Methyl acrylate | 0.88 | 0.67 | 1.1 |
| 2-hexyl-1-decanol | Methyl acrylate | 0.69 | 0.64 | 0.74 |
| Methoxypropylphenol | Methyl acrylate | No reaction |  |  |
| Isoeugenol | Methyl acrylate | No reaction |  |  |
| 4-methoxybenzyl alcohol | Methyl methacrylate | 0.44 | 0.40 | 0.47 |
| Furfuryl alcohol | Methyl methacrylate | 0.36 | 0.25 | 0.48 |
| Tetrahydrofurfuryl alcohol | Methyl methacrylate | 0.35 | 0.31 | 0.38 |
| Methoxypropylphenol | Methyl methacrylate | No reaction |  |  |
| Isoeugenol | Methyl methacrylate | No reaction |  |  |

**4. Conclusions and perspectives**

Industrially appealing conversions and ester concentrations in solventless conditions were reached in this study. Progression curves were simultaneously used as input to estimate second order reaction rates and their confidence intervals based on nonlinear regression techniques. Larger scale production is currently under investigation for production of kg scale quantities.

**References**

[1] V. Athawale, N. Manjrekar, M. Athawale, Enzymatic synthesis of chiral menthyl methacrylate monomer by *Pseudomonas cepacia* lipase catalysed resolution of (+-)-menthol, J Mol Catal B-Enzym, 16 (2001) 169-173.

[2] V. Athawale, N. Manjrekar, M. Athawale, Lipase-catalyzed synthesis of geranyl methacrylate by transesterification: study of reaction parameters, Tetrahedron Lett, 43 (2002) 4797-4800.

[3] S. Warwel, G. Steinke, M.R. Klaas, An efficient method for lipase-catalysed preparation of acrylic and methacrylic acid esters, Biotechnol Tech, 10 (1996) 283-286.

[4] A.E.V. Petersson, L.M. Gustafsson, M. Nordblad, P. Börjesson, B. Mattiasson, P. Adlercreutz, Wax esters produced by solvent-free energy-efficient enzymatic synthesis and their applicability as wood coatings, Green Chem, 7 (2005) 837-843.

[5] M.B. Ansorge-Schumacher, O. Thum, Immobilised lipases in the cosmetics industry, Chem Soc Rev, 42 (2013) 6475-6490.

[6] A. Heeres, K. Vanbroekhoven, W. Van Hecke, Solvent-Free Lipase-Catalyzed Production of (Meth)acrylate Monomers: Experimental Results and Kinetic Modeling, Biochem Eng J, DOI:10.1016/j.bej.2018.11.011, (2019).