Chemical Engineering Journal 312 (2017) 106–117

Contents lists available at ScienceDirect

Chemical Engineering Journal

journal homepage: www.elsevier.com/locate/cej

Pilot-scale validation of Enzymatic Reactive Distillation for butyl butyrate production

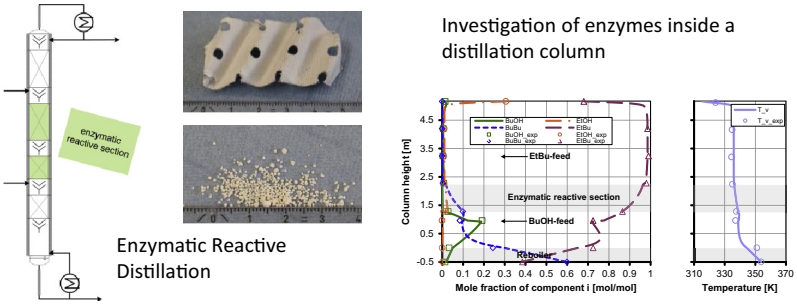
Matthias Wierschem [a,*], Stefan Schlimper [a], Rene Heils [b], Irina Smirnova [b], Anton A. Kiss [c,d], Mirko Skiborowski [a], Philip Lutze [a]

[a] Laboratory of Fluid Separations, TU Dortmund University, Emil-Figge-Str. 70, 44227 Dortmund, Germany
[b] Institute of Thermal Separation Processes, TU Hamburg, Eißendorfer Str. 38, 21073 Hamburg, Germany
[c] AkzoNobel Research, Development & Innovation, Process Technology SRG, Zutphenseweg 10, 7418 AJ Deventer, The Netherlands
[d] Sustainable Process Technology Group, Faculty of Science and Technology, University of Twente, PO Box 217, 7500 AE Enschede, The Netherlands

HIGHLIGHTS

- Butyl butyrate synthesis by Enzymatic Reactive Distillation is possible.
- Established rate-based model to describe Enzymatic Reactive Distillation.
- First time validation for an Enzymatic Reactive Distillation process model.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 20 July 2016
Received in revised form 11 November 2016
Accepted 19 November 2016
Available online 21 November 2016

Keywords:
Biocatalysis
Hydrodynamics
Lipase
Modeling
Process intensification
Reactive distillation

ABSTRACT

For enzyme-catalyzed reactions, batch processes using stirred tank reactors are the state-of-the-art production mode. The yield of the process may be limited by reaction equilibrium, product inhibition of the enzyme, low concentrations and possibly low reaction rates, while the recovery of the product may be limited due to thermodynamic constraints such as azeotropes. Using enzymes in an integrated reactive distillation process can overcome these limitations and provides a cost advantage over classic batch reactor processes.

The aim of this paper is i) to report the successful pilot-scale experimental validation of an Enzymatic Reactive Distillation (ERD) process for the synthesis of butyl butyrate and ii) to establish a rate-based model for conceptual process design which can be quickly adapted to other systems.

The main novelty is the application of a continuous RD column with enzymes as a heterogeneous catalyst provided in two different types of catalytic packing: loosely filled immobilized enzyme beads in standard packings with catalyst pockets and gauze packings with catalytic coating.

Experimental pilot-scale experiments show the feasibility of ERD and allow the comparison of the different packing types based on catalytic performance as well as stability. Furthermore, these experiments are used to validate a predictive rate-based model to describe ERD which can be used to check the sensitivity of process and design parameters as well as to provide a quick adaption to other systems for quick evaluation.

* Corresponding author.
E-mail address: matthias.wierschem@bci.tu-dortmund.de (M. Wierschem).

http://dx.doi.org/10.1016/j.cej.2016.11.127
1385-8947/

1. Introduction

Biocatalysis underpins some of the oldest chemical transformations known to humankind, and it has become a key component in the toolbox of chemists and chemical engineers, allowing new green chemistry and highly productive processes to be developed [1]. Enzyme-catalyzed processes are used in many industrial processes, as for example the synthesis of enantiomerically pure chemicals which are important as intermediates in the pharma- and agro-industry [2]. The pharmaceutical and fine chemicals industry is demanding for economically more attractive processes [2]. Still, the most commonly used production mode for enzyme-catalyzed reactions is based on batch processes using stirred tank reactors [3]. These processes lack in productivity and product purity [1]. A key problem is the increasing concentration of the reaction products that can cause inhibitory or toxic effects or promote unfavorable equilibria. In such cases, *in-situ* product removal is used to remove the product as soon as it is formed in order to overcome the constraints and increase the productivity and space-time-yield of the bioprocess [4]. In fine chemicals or pharmaceutical production, continuous production can significantly enable increased throughput, process safety, greener production [5], process automatization and control, easier modeling, smaller hold-up of solvents, improved heat transfer and a cost reduction in operation and installation [6].

Integrated and/or intensified processes are important tools for the successful and cost-efficient realization – one technique of process intensification is reactive distillation (RD) which realizes the integration of reaction and product removal by distillation in one apparatus, which opens up for potential higher conversion, selectivity, efficiency and capacity [7]. Using enzymes in combination with a RD process instead of a classic batch process can overcome chemical and phase equilibrium, and can deliver a cost-effective alternative to classic batch processes [8]. Heils et al. (2015) investigated an enantio-selective biocatalytic reaction carried out in a fully integrated batch RD setup [9].

However, as RD using chemical catalysts either homogeneous or heterogeneous has been presented many times before [10,11], while to the best of our knowledge there are no experimental reports on continuous Enzymatic Reactive Distillation (ERD) processes. Furthermore, different models such as equilibrium or rate-based approaches for RD using chemical catalysts have been developed and successfully used to evaluate feasibility, cost competitiveness or process optimization [12]. However, such models do not yet exist for ERD processes. Therefore, this study aims to fill this gap i) by being the first to report the pilot-scale experimental validation of an ERD process based on the synthesis of butyl butyrate and ii) by establishing and validating a rate-based model of the ERD.

The chemical model system used for this study is the production of butyl butyrate (BuBu), a volatile ester with a pleasant aroma, used in the flavor industry to create sweet fruity flavors similar to that of pineapple. This transesterification reaction of ethyl butyrate (EtBu) with *n*-butanol (BuOH) forming ethanol (EtOH) uses lipase as catalyst (Eq. (1)). This chemical system is suitable for RD according to the feasibility scheme of Shah et al. (2012) [13].

$$\mathrm{EtBu} + \mathrm{BuOH} \rightleftharpoons \mathrm{BuBu} + \mathrm{EtOH} \quad (1)$$

Among the enzymes used industrially, the B-component lipase from the yeast *Candida antarctica* (CalB) is a particularly efficient and robust lipase catalyzing a large diversity of organic reactions, including transesterification [14]. The enzymatic catalyst is immobilized in two different configurations, either as enzyme beads sandwiched in structured packing or as enzyme containing silica-gel based coating applied onto structured packing (Fig. 1). Both catalytic packings are introduced in the pilot-scale RD column at the Laboratory of Fluid Separations, TU Dortmund University, for experimental investigation.

A comprehensive rate-based model is extended from the former developed rate-based model [15], incorporating mass and energy transfer, packing properties and the reaction kinetics. The main approach is to use "offline" measurement of kinetics and thermodynamics at lab scale together with hydrodynamic investigations of the influence of enzyme as beads or as coating in a binary non-reactive system. All these models are afterwards incorporated into one rate-based model. This model allows analyzing the experimental results to gain more insights into the experiments. Therefore, a sensitivity analysis was performed to efficiently identify sensitive process and design variables as literature examples show [16–18], which can be used for future improvement as well as enable efficiently the identification of a feasible operating window.

2. Problem statement

For the evaluation of ERD processes, reliable process models are needed to provide predictions of operating states, scale-up possibilities and production cost calculations. To fill this gap, we propose to establish such a model on a fundamental basis of experiments as described in a recent publication [19]. The steps to an evaluation of this technology are: 1) collection of fundamental data (and experiments), 2) identification of an operating window, 3) development of a mathematical model, 4) model-based process analysis, 5) equipment-based experiments, 6) model validation and 7) optimization of the process.

The collection of fundamental data including property data [20] and the reaction kinetics [21] was presented recently. In this paper, we address the investigations of packing properties, we identify the operating window and we develop a mathematical model, followed by experiments which were carried out in a pilot-scale ERD column and a conventional distillation column. The aim is to propose an accurate rate-based model that describes ERD and to provide an experimental basis to prove the feasibility of ERD processes. The packing properties and correlations like hold-up, mass transfer and specific surface area, are required, but not available for the coated packing used in this study and are therefore investigated in a distillation set-up for a close-boiling binary system of *iso*-butanol (IBU) and BuOH and broadened afterwards to a rate-based model with the Maxwell-Stefan approach.

3. Experimental

In the experimental part of the work we address the materials and methods that were used to investigate the ERD, including descriptions of the ERD column and gas chromatographic (GC) analysis. A binary distillation system is used to ascertain properties of the used coated packing. The ERD experiments are conducted to show the feasibility of the ERD and to be able to validate the ERD model.

As both, reaction and separation, occur simultaneously in a RD unit, there must be a proper match between the temperatures and pressures required for reaction and separation translated into an overlapping window of the operating conditions [7]. Fig. 2 illustrates the temperature and pressure range for the ERD process described in this study. This assessment is required for any experimental work. More details are provided in a subsequent section.

3.1. Material & methods

3.1.1. Chemicals

Table 1 provides the list of used chemicals, including the substance name, its purity and the producer, as well as the application area.