Separation and Purification Technology 169 (2016) 1–8

Contents lists available at ScienceDirect

Separation and Purification Technology

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

Recovery of *cis,cis*-muconic acid from organic phase after reactive extraction

Jannick Gorden [a], Tim Zeiner [b], Gabriele Sadowski [a], Christoph Brandenbusch [a,*]

[a] Laboratory of Thermodynamics, Technische Universität Dortmund, D-44227 Dortmund, Germany
[b] Laboratory of Fluid Separations, Technische Universität Dortmund, D-44227 Dortmund, Germany

ARTICLE INFO

Article history:
Received 15 February 2016
Received in revised form 23 May 2016
Accepted 26 May 2016
Available online 27 May 2016

Keywords:
Downstream processing
Reactive extraction
Recovery
Re-extraction
cis,cis-muconic acid

ABSTRACT

Reactive extraction has been shown as an applicable first step in the downstream processing for the recovery of dicarboxylic acids from aqueous solutions, leading to yields of $X_{RE} = 0.95 \pm 0.05$ for *cis,cis*-muconic acid. A next step towards a downstream processing concept is the examination of strategies to recover the dicarboxylic acid from the organic phase. A reasonable strategy has to lead to high yields and allow for a recycle of the organic phase for further reactive extraction steps. This work presents two recovery strategies for the *cis,cis*-muconic acid after reactive extraction. A pH-shift uses the strong pH dependency of the reactive extraction itself. A buffered aqueous phase as re-extraction phase leads to a yield of $X_{REEX} = 0.99 \pm 0.080$ at pH > 7. The second approach is the addition of water soluble amines as an additional reactive component. A complex of water soluble amines and the acid is re-extracted into an aqueous phase. Propylamine showed the best performance ($X_{REEX} = 1 \pm 0.069$) of all water soluble amines investigated. An analysis of the distribution behavior of the water soluble amines showed that a recycle of the organic phase for further reactive extraction steps is feasible for both strategies. The results allow for a further development of an in situ downstream processing concept for biocatalytic produced dicarboxylic acids.

1. Introduction

Dicarboxylic acids are an evolving group of substances with the potential to serve as chemical building blocks, e.g. within the production of biodegradable polymers [1–4]. This fact is based on their high reactivity due to the two terminal carboxylic groups. Especially within the last years the biocatalytic production of dicarboxylic acids has been investigated intensively and upstream processes already achieve titers suitable for an industrial production [5–7]. In contrast, the downstream processing has not yet kept up with this development and can thus be stated as the bottleneck towards an industrial application of bio catalytically produced dicarboxylic acids. One reason is the high effort required to recover a hydrophilic product from a complex aqueous (fermentation) broth which results in cost intensive purification concepts [8]. Thus, there is an immediate need for an economic and selective product capture step to recover the dicarboxylic acid from the fermentation broth. One promising approach described recently is the application of a reactive extraction (RE) for this purpose [9]. By combining the beneficial attributes of an extraction and a reaction, the distribution behavior within a liquid-liquid extraction can be favored towards a selective recovery of the product. In the respective case this is achieved by introducing a water insoluble amine, building a hydrophobic complex with the acid, which can then be extracted into an organic phase [10–14]. Reactive extraction of dicarboxylic acids has been shown to be applicable for various dicarboxylic acids, e.g. malonic acid [15–17], glutaric acid [18], succinic acid [15–17,19–23], fumaric acid [15–17], malic acid [18,24], maleic acid [15–18], itaconic acid [25–27] and *cis,cis*-muconic acid (*CC*MA) [9]. However, the crucial step towards an applicable downstream process is not only the initial RE of the acid, but also a re-extraction (REEX) of the acid from the organic phase leading to the pure acid in an aqueous phase for further processing. This recovery step is very poorly investigated. Problems mainly arise from the fact that a recovery of the acid from the organic phase has to be at a high yield with a simultaneous consideration of a recycle of all process streams used for RE and REEX. In general, five potentially suitable options are discussed in literature [12,21,28–32]:

* Corresponding authors.
E-mail addresses: tim.zeiner@bci.tu-dortmund.de (T. Zeiner), christoph.brandenbusch@bci.tu-dortmund.de (C. Brandenbusch).

http://dx.doi.org/10.1016/j.seppur.2016.05.032
1383-5866/

Nomenclature

Symbol	Definition (unit)	Symbol	Definition (unit)
b	molality (mol·kg^{-1})	m	mass (g)
w	weight fraction (–)	T	temperature (°C)
X	yield (–)	Z	molar ratio (–)
n	amount of substance (mol)	K	distribution coefficient (–)
		pK	negative decimal logarithm of K (–)

1. REEX using a temperature gradient
2. Change of the organic solvent
3. REEX using a stronger acid
4. REEX via pH-shift
5. REEX using trimethylamine

The REEX using a temperature gradient (1) was investigated by Keshav et al. [29] for the recovery of propionic acid (mono-carboxylic acid) from *iso*-butyl methyl-ketone which lead to a yield of 66–88%. A change of the organic solvent (2) shifts the complex into a different solvent but does not allow for a recovery of the pure acid. Within option 3 a strong aqueous acid solution is used for the REEX of the carboxylic acid from the organic phase. The stronger acid forms a complex with the extractant (amine) and the carboxylic acid will preferentially partition into the aqueous phase. The problem within this strategy is the irreversible loading of the amine extractant with the strong acid and the high salt fraction within the process, making a recycle of the organic RE phase impossible. Option 4 makes use of the strong pH dependency of the RE. It was previously shown [9] that a RE using pure amine as extractant is only possible if the pH is lower than the smallest pK_a of the dicarboxylic acid. An aqueous phase set to a pH higher than the pK_a of the acid thus leads to a breakup of the complex and a subsequent REEX of the acid into an aqueous phase. The most promising strategy (Option 5) is the use of a trimethylamine solution for REEX [12,21,32,33]. For propionic acid (mono-carboxylic acid) a complete recovery of the acid from the organic phase was reported by Keshav et al. [29]. Kurzrock et al. [21] investigated the REEX of succinic acid from octanol and mixtures of 1-octanol and 1-hexanol, both containing an amine as extractant. This REEX of succinic acid led to a complete recovery of the acid from the organic phase into the aqueous trimethylamine solution. The resulting hydrophilic complex of trimethylamine and *CC*MA was broken via an evaporation-based crystallization [21]. However, the use of an aqueous trimethylamine solution has some disadvantages for the industrial application. Trimethylamine is corrosive and gaseous at standard conditions and by that highly volatile. In our previous work [9] we already assumed that the group of amine candidates for REEX can be extended to water soluble amines (WSA) in general. In order to circumvent the problems associated with the use of an aqueous trimethylamine solution (corrosivity, high volatility) and allow for an understanding of the REEX mechanism, two different strategies were investigated within this work: (1) the REEX via pH-shift and (2) the REEX using WSA's. Within the pH experiments, the aqueous phases were set to a certain pH by the use of a citrate buffer. Four different WSA's (with differing water solubility) each applied in various concentrations were tested within the second set of experiments. The systematic extension of the REEX strategy (5) to WSA's in general, in combination with the pH experiments allow for a better understanding of the mechanism of the reactive extraction itself. Within this work, *CC*MA was chosen as example, due to its relevance for the chemical industry as a potential precursor for adipic acid [34–36] and other polymerization and esterification reactions [37,38]. The biocatalytic production of *CC*MA using whole-cell biocatalysis, is well described in recent literature [34,36–40]. Fig. 1 presents the recovery of the *CC*MA for the two investigated REEX strategies as a principle scheme, for a better understanding of the desired downstream concept.

2. Materials and methods

2.1. Chemicals

Ethyl oleate (EO) was purchased from TCI (Tokyo, Japan). Tri-n-octylamine (T-C8) was purchased from AlfaAesar (Karlsruhe, Germany). Propylamine (M-C3), butylamine (M-C4), hexylamine (M-C6), tri-n-propylamine (T-C3), phosphoric acid, dihydrogen orthophosphate, 1-dodecanol, citric acid and *CC*MA were purchased from SigmaAldrich (St.Louis, USA). Acetonitrile and disodium phosphate were purchased from VWR Chemicals (Darmstadt, Germany). The *CC*MA was recrystallized before usage to separate the acid from impurities. Therefore, *CC*MA was dissolved in pure Millipore water at T = 50 °C. The hot solution was filtered through a Pall Sapor-100 0.1 μm filter produced by PALL Corporation (Michigan, USA) using a MD 1C vacuum pump manufactured by Vacuubrand (Wertheim, Germany). Afterwards the filtrate was directly transferred into a standard glass bottle and cooled to T = 5 °C using a water/ice bath. The recrystallized *CC*MA was then separated using a Pall Sapor- 100 0.1 μm filter. All other chemicals were used in the delivered purity without further purification. Table 1 provides detailed information about the chemicals used in this work.

2.2. Analytical methods

The concentration analysis of the *CC*MA in the aqueous phase was performed via high pressure liquid chromatography (HPLC) as described by Gorden et al. [9] using an Agilent 1200 Series HPLC (Santa Clara, USA) and a series of a Zorbax SB-C18, 4.6 · 12.5 mm, 3.5 μm guard column, a Zorbax SB-C18, 4.6 · 50 mm, 1.8 μm, and a Zorbax Extend-C18, 4.6 · 50 mm, 1.8 μm column [by Agilent Technologies (Santa Clara, USA)]. The temperature was kept constant at 40 °C. The initial eluent at a volume flow of 0.5 mL min^{-1} is composed of a 50 mM phosphate buffer (PB) solution at a pH of 2 and acetonitrile (ACN) (90/10 V_{PB}/V_{ACN}). Two gradients were applied to obtain an optimal separation result. The flow was changed at t = 1 min (0.5 → 1 mL min^{-1}) and the eluent ratio was changed at t = 1.8 min (V_{PB}/V_{ACN}: 90/10 → 60/40). A diode array detector (DAD) set to a wavelength of 200 nm was used for detection. The injected sample amount was always 5 μL.

The concentration of the *CC*MA within the organic phase was calculated via mass balance.

For experiments investigating the REEX of the *CC*MA using a WSA, the concentration of the WSA in the organic phase was analyzed via gas chromatography (GC) on an Agilent 7890A GC-system (Santa Clara, USA). An Agilent Innowax column, 30 m·320 μm, 0.25 μm (Santa Clara, USA) and a flame ionization detector (FID) was used for the analysis. Hydrogen was used as carrier gas at a constant volume flow of 1 mL min^{-1}. Injection volume was 1 μL with a split ratio of 20:1. After an initial hold of 2 min at 45 °C the oven was heated to a temperature of 260 °C with a heating rate