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STATE-OF-THE-ART RECOVERY OF FERMENTATIVE ORGANIC ACIDS BY IONIC LIQUIDS: AN OVERVIEW

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The main achievements of liquid–liquid extraction (LLE) of fermentative organic acids from their aqueous sources using a diverse range of ionic liquids are summarized since the first study appeared in 2004. The literature survey is organized in consideration of the distinct chemical structures of the organic acids. The acids discussed include mono– or dicarboxylic ones (butyric, L-malic and succinic acids), acids bearing both carboxyl and hydroxyl groups (L-lactic, citric and mevalonic acids), and volatile organic acids (mainly acetic acid). Information is given about ionic liquids applied in recovery, and the resultant extraction efficiencies and partition coefficients. As the topic is novel and experimental studies scarce, the selection of the ionic liquids that were tested still seems random. This may well change in the future, especially after improving the ecological and toxicological characteristics of the ionic liquids in order to bring about an "*in situ*" method of extraction without harming the microbial producers of the organic acids.

Keywords: extraction, ionic liquid, organic acid, recovery, re–extraction

1. Introduction

Room temperature ionic liquids (ILs) exist as molten salts at ambient temperature and consist entirely of ions, usually a charge–stabilized organic cation and an inorganic or organic anion. ILs can be tailored to a wide variety of applications by combining different ions [1] and for this reason they are often called "designer solvents". ILs exhibit a broad range of unique properties, including negligible vapor pressure, high thermal stability and low chemical reactivity [2]. The union of these particular properties, together with finely tunable density, viscosity, polarity and miscibility with other common solvents favor the application of ILs in different kinds of separation and reaction processes [3–8].

Considering the benefits that arise from the properties of ILs, Matsumoto et al. [9] first proposed an environmentally friendly system for the extraction of fermentative L-lactic acid. They used hydrophobic $[C_nC_1im][PF_6]$ instead of volatile organic solvents as diluents of reactive organic bases. These ILs proved to be nontoxic towards the lactic acid producing bacterium *Lactobacillus rhamnosus*, but provided low degrees of solubility of the reactive amines which resulted in insufficient levels of extraction efficiency. Nevertheless, these results suggest possible applications of ILs in extractive fermentations.

2. Discussion on the organic acids extracted and the ionic liquids applied

2.1. Butyric acid and phosphinate–based ILs

The most remarkable results regarding the partition coefficient of an organic acid in an IL have been documented with regards to the extraction of butyric acid, the four–carbon fatty acid, with phosphinate-based ([Phos]) ILs. $[P_{6,6,6,14}]$[Phos] and a novel ammonium phosphinate, $[C_nC_nC_nC_1N]$[Phos], were studied [10-11]. Distribution coefficients of about 80 were obtained using the low concentrations of butyric acid, and the extraction efficiency was just as high in the pure (water saturated) IL as in the IL/water/dodecane reversed micellar solution. The ammonium phosphinate absorbed a relatively high amount of water until saturation was achieved, *ca* 21 wt%. (about 12 water molecules per ion pair of the IL), which implies that an aqueous biphasic system was formed.

2.2. Dicarboxylic acids and phosphonium- or imidazolium-based ILs

Among phosphonium-based ILs, $[P_{6,6,6,14}]$Cl seems the most suitable extractant for the recovery of low and moderate concentrations of dicarboxylic L-malic acid in aqueous solutions [12]. The other phosphonium-based ILs and higher acid concentrations entrain third-phase formation, especially in the case of $[P_{6,6,6,14}]$[Phos] when a large amount of the acid content (*ca* 40%) remains

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*Correspondence: konstantzatonova@yahoo.com uncovered in both phases. The $[P_{6,6,6,14}]Cl$–rich phase is also the best extractant for another dicarboxylic acid, succinic acid [12]. Extractions with [Dec]- and [Phos]–based ILs resulted in a substantial amount of undetectable acid in both phases, which was attributed to the formation of complexes between the organic acid and the extractants that were not quantified.

More recently succinic acid attracted special attention in a comprehensive study where the extraction was carried out by aqueous biphasic systems (ABS) of alcohols/salts or imidazolium-based ILs/salts [13]. Successful recovery was achieved by both systems. Succinic acid preferentially migrates to the IL–rich phase in all systems formed of $[C_6C_1im]Br$ and a kosmotropic salt (phosphate, sulfate, carbonate or citrate). The IL salted out by $(NH_4)_2SO_4$ or K_2CO_3 exhibited the highest levels of extractability. The pH values of these systems were quite different. The pH of the system with $(NH_4)_2SO_4$ was 3.43 which is below the pK_a values of succinic acid ($pK_{a1} = 4.21$, $pK_{a2} = 5.72$), while pH = 10.50 for K_2CO_3 greatly exceeded the $pK_a s$. This suggests that unlike the aqueous biphasic systems with alcohols, the extraction capacity of the IL/salts systems towards succinic acid is not pH–dependent and is most likely related to the proper nature of the solvent (IL/salt) and the solute (acid). For the same IL, $[C_6C_1im]Br$, an excellent solvating capacity to the lactic acid was reported [14] so that the acid could be extracted from a concentrate of white wine. This way the extraction efficiencies of the ABS of $[C_6C_1im]Br/(NH_4)_2SO_4$ or K_2CO_3 are comparable to those obtained with the hydrophobic IL $[P_{6,6,6,14}]Cl$ [12]. Moreover, the re–extraction efficiency achieved was superior at ~71%. Succinic acid was obtained in a crystalline form by direct precipitation with sodium hydroxide.

2.3. Acids with both hydroxyl and carboxyl groups and phosphonium- or imidazolium-based ILs

Different types of phosphonium-based IL biphasic systems were applied for L–lactic acid recovery. An extraction efficiency of above 80% was achieved by using either pure $[P_{6,6,6,14}][Phos]$ [12] or a mixed biphasic system of $[P_{6,6,6,14}]Cl$ and an inorganic kosmotrope, $MgSO_4$ [15]. The kosmotropic salt engages more water molecules when hydrated thus rendering the microenvironment of the acid more hydrophobic which favors the undissociated form of acid suitable for extraction. All extraction systems of phosphonium-based ILs with long side chains suffer from the common disadvantage of forming stable emulsions or a third phase between the IL–rich phase and aqueous solution. This drawback is avoided by applying ILs of an imidazolium cationic moiety, however, in the majority of the cases these ILs exhibit low levels of extraction efficiency towards lactic acid [9,16] and other acids bearing both hydroxyl and carboxyl groups (citric and mevalonic acids) [16].

An advantageous ABS of imidazolium saccharinate, that possesses a long side chain, $[C_{8/10}C_1im][Sac]$, has been exploited lately and it was shown that when it is combined with an inorganic kosmotropic salt (that retains water from solubilization into the IL–rich phase) an extraction efficiency of 81% and partition coefficient of 5.5 could be achieved [17]. The extraction yield of lactic acid was as high as 90% in a two–step recovery by $[C_8C_1im][Sac]$ with or without the addition of a kosmotropic salt ($MgSO_4$). Moreover, successful acid re–extraction of 95% from the IL–rich phase was attained by means of a solution containing an alkaline kosmotrope, K_2HPO_4.

2.4. Volatile fatty acids and phosphonium-based ILs

Apart from culture broths, fermented wastewater streams still represent an unexploited source of platform chemicals, including volatile organic acids. Volatile fatty acids are versatile carboxylic acids involved in the synthesis of bioplastics and other value–added chemicals [18]. The composition of fermented wastewater typically contains ~1 wt% of volatile fatty acids, but also a significant amount of various dissolved salts. The low concentrations of the volatile fatty acids and the large quantity of inorganic salt–originating ions result in pH–values of between 4 and 6, which are in favor of the deprotonated acid form and thus do not support complexation with the IL. The distribution of acetic acid between model solutions with or without salts and different solvents, including phosphonium-based ILs, was recently studied [19]. Similarly to the butyric and lactic acids [10,20], the low concentration of acetic acid and the use of $[P_{6,6,6,14}][Phos]$ were the best conditions to obtain the highest partition coefficient in the IL–rich phase starting from an idealized aqueous solution containing only the acetic acid. In the presence of salts (KCl, Na_2SO_4 or Na_2HPO_4), however, the partition coefficients reported for $[P_{6,6,6,14}]Cl$ were the highest in the series of ILs tested and exceeded even those obtained in the classical extraction by trioctylamine (TOA)/n-octanol. $[P_{6,6,6,14}]Cl$ as a solvent has an inevitable drawback related to its measurable level of leaching into the aqueous phase due to the hydrophilicity of the $[Cl]^-$. Contrary to $[P_{6,6,6,14}]Cl$, $[P_{6,6,6,14}][Phos]$ and $[P_{6,6,6,14}][N(CN)_2]$ were found to be highly stable as significant leaching was not detected in the aqueous phases [19]. Extraction by $[P_{6,6,6,14}][Phos]$, however, was strongly affected by the ions of the salts present in the feed, while $[P_{6,6,6,14}]Cl$ and $[P_{6,6,6,14}][N(CN)_2]$ kept extraction capacities constant for acetic acid. When the source contained different acids, mimicking actual fermented wastewater, it was found that the growing hydrophobic domain in the acid leads to higher degrees of extraction. Butyric acid was the most extracted acid from the fermented wastewater, while lactic acid was the most challenging acid to extract. By modifying the solvent properties of $[P_{6,6,6,14}][Phos]$ by sparging pressurized CO_2, a further increase in the extractability of acetic acid was observed

[21]. The effect was attributed to the altered structure of the fluid which becomes more accessible for the acetic acid. This finding constitutes a general concept for the improvement of extraction processes other than those involving volatile fatty acids.

ILs can act as solvents and simultaneously mediate reactive extraction to valorize low–titer volatile fatty acids. This has been recently shown through an IL–mediated esterification of acetic acid recovered from dilute aqueous streams [22]. The acids produced in anaerobic digestion or fermentation were transferred to a nonvolatile hydrophobic phase where they reacted with an alcohol (ethanol) in order to generate volatile, value–added esters of low solubility. $[P_{6,6,6,14}]$–ILs were selected for their potentially high extracting capacity and hydrophobicity. Their hydrophobic character provides a water-excluding site for esterification and a nonvolatile carrier for the evaporation of the ester produced. Significant accumulation of acetic acid in the IL was achieved by using $[P_{6,6,6,14}][N(CN)_2]$, but this was mainly due to the exchange of $[N(CN)_2]^-$ for the acetate anion as the dicyanamide anion was found to hydrolyze under the extraction conditions used, including at an elevated temperature (75 °C). Contrary to the extraction, $[P_{6,6,6,14}][N(CN)_2]$ and $[P_{6,6,6,14}]Cl$ appeared to be the worst media for performing esterification, while the best was $[P_{6,6,6,14}][Tf_2N]$, which, however, is poor and costly extractant. Thus an IL of combined anions, $Cl^- + [Tf_2N]^-$, was tested which could be used in a multistage way. Starting from an aqueous stream of 0.33 mol dm^{-3} acetic acid, 0.44 mol dm^{-3} accumulated in the mixed $[P_{6,6,6,14}]Cl+[Tf_2N]$ which allowed an esterification conversion of 56% to be achieved over 30 min.

3. Conclusion

ILs are commonly considered more sustainable than classical organic solvents. It is well known that the toxicity level of conventional solvents to microbes limits their compatibility with fermentation broths. However, the label of "green solvent", assigned to the ILs, has led to the delusion that they are nontoxic and biodegradable, which is not true about some of the most employed ILs. For example, the commonly used $[P_{6,6,6,14}]Cl$ may be regarded as toxic in aquatic environments exhibiting much higher levels of ecotoxicity compared to ordinary organic solvents [23]. The biocompetitiveness and biodegradability of ILs are not still convincingly argued for [24-25]. The need for novel extractants with improved characteristics from ecological and toxicological standpoints can be put forward. By taking into account that aqueous streams and bioorganics are treated, the environmental impact of ILs should be resolved as a result of future studies.

SYMBOLS

IL's cationic moiety:	
$[C_nC_1im]$	1-alkyl-3-methylimidazolium
$[C_nC_nC_nC_1N]$	trialkylmethylammonium
$[P_{6,6,6,14}]$	tetradecyl(trihexyl)phosphonium
IL's anionic moiety:	
[Dec]	decanoate
$[N(CN)_2]$	dicyanamide
[Phos]	bis(2,4,4-trimethylpentyl)phosphinate
[Sac]	saccharinate (which is a benzoic sulfimide)
$[Tf_2N]$	bis(trifluoromethylsulfonyl)imide
Other:	
TOA	trioctylamine

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