

Ionic Liquid-based Thermomorphonic Solvent Systems for Biocatalytic Reactions

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Introduction

Thermomorphonic solvent systems (TMS) are specific solvent mixtures that exhibit a temperature-dependent miscibility gap, which allows the utilization of a reversible macroscopic phase change between mono- and multiphase conditions.^[1] For systems with a UCST-type phase behavior, monophasic reaction conditions at higher temperatures and an easy recycling of the biocatalyst after phase separation at lower temperatures

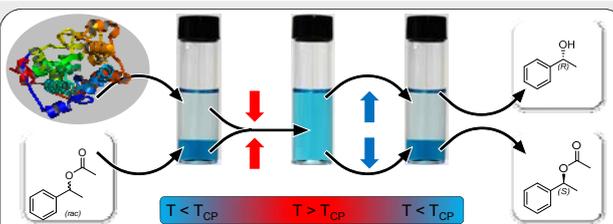


Fig. 1: Kinetic resolution reaction in a thermomorphonic solvent system composed of [Bmim][BF₄], water and NaPi-salt. T_{CP} = cloud point Temperature.

can be achieved (Fig. 1). In this study various ionic liquid/salt/water-mixtures were screened regarding their liquid-liquid phase equilibria (cf. Fig. 3) and evaluated with selected biocatalytic reactions. Especially tetrafluoroborate-based ionic liquids show good to excellent catalytic activities and recyclabilities. The resulting hydrophobic solvent systems facilitate high solubilities of the reactants.

Results and Discussion

IL-based Aqueous Biphasic Systems

The phase behavior of ionic liquid-inorganic salt-water mixtures as IL-based aqueous biphasic systems (IL-ABS) was first investigated in 2003 by ROGERS et al.^[2] The interactions of the three components is typically displayed in a ternary phase diagram (Fig. 2). Here the so called binodal curve illustrates the border between the homogenous (1-PS) and the heterogeneous (2-PS) regime.

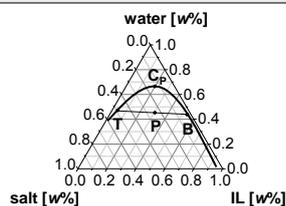


Fig. 2: Illustration of a ternary phase diagram of an IL-ABS. C_p = upper critical solution temperature (UCST).

By changing the temperature, it is possible to shift the binodal curve into the homogeneous regime (Fig. 3). With the knowledge of the temperature dependent phase behavior it is possible to separate the biocatalyst from the IL-rich phase to reuse it in a new reaction.^[3]

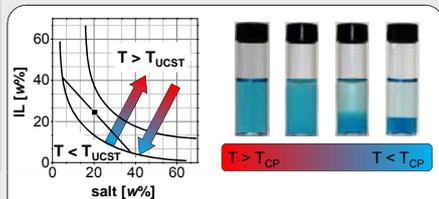


Fig. 3: Temperature dependent miscibility gap of IL-ABS.

Use of IL-ABS for biocatalytic reactions

In this study, the kinetic resolution reaction of racemic 1-phenylethanol by *Candida antarctica* lipase B (CalB) was investigated as a model reaction (Fig. 4).

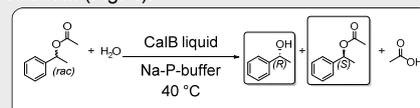


Fig. 4: Enantioselective kinetic resolution reaction.

In contrast to classical biphasic systems (Fig. 5) significantly higher reaction rates were obtained with an IL-ABS-system. In addition, higher solubilities of the reactants are possible with thermomorphonic solvent systems (TMS) in comparison to aqueous media. The half live stability of CalB in the [Bmim][BF₄]-ABS-system is about 30 hours (Fig. 6).

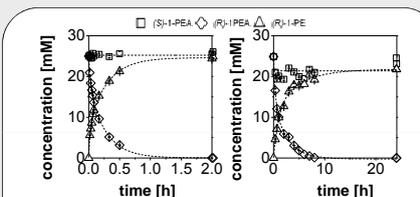


Fig. 5: Higher reaction rates in the IL-ABS (left) can be achieved in comparison to an organic 2-PS (MTBE, right).

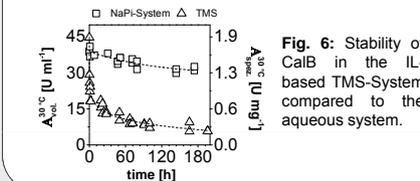


Fig. 6: Stability of CalB in the IL-based TMS-System compared to the aqueous system.

Recycling and IL-TMS-System library

After cooling the [Bmim][BF₄]-TMS-system it was possible to reuse the aqueous enzyme-rich phase to perform several recycling runs (Fig. 7). The conversion of the reactions remained high over 3 to 4 runs. After 6 runs a loss of 50 % conversion was observed.

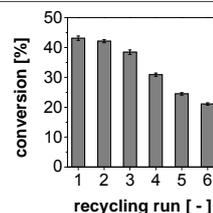


Fig. 7: Results of catalytic recycling runs (reaction conditions: 30 min per run at 40 °C).

Various other ionic liquid/salt/water-mixtures were screened and evaluated regarding their applicability (Table 1).

Table 1: Ranking of different IL-TMS examined in this study.

no	ionic liquid	secondary solvent	ranking
1	[Bmim][BF ₄]	150 mM NaPi-buffer	++++
2	[Bpy][BF ₄]	233 mM NaPi-buffer	++++
3	[Emim][BF ₄]	567 mM NaPi-buffer	++
4	[Bmim][NO ₃]	350 mM NaPi-buffer	0
5	[Emim][Br]	470 mM NaPi-buffer	0
6	[Bmim][Br]	333 mM NaPi-buffer	0
7	[Bmim][Cl]	-	-

++++ indicates that all parameters were accomplished (solubility of the substrate, UCST-type phase behaviour, high reaction rates), ++ indicates an immiscibility of the substrate, 0 indicates a small phase separation after cooling and an immiscibility of the substrate, - indicates that no phase separation occurs at 40 °C.

Conclusion

- Pyridinium- and imidazolium-based ionic liquids were investigated for the use as thermomorphonic solvent systems.
- An enantioselective model reaction was carried out in IL-based TMS-systems.
- The IL-based TMS-systems facilitate a considerable faster conversion than classical organic biphasic systems.
- The investigation of the recycling of the biocatalyst showed a practically application for three to four times.
- Further biocatalytic reactions were successfully carried out in thermomorphonic solvent systems (data not shown).

References

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