Universität Rostock

Traditio et Innovatio

Biocatalysis in thermomorphic solvents

A. Gummesson, J. von Langermann and U. Kragl

University of Rostock, Institute of Chemistry, Albert-Einstein-Straße 3A, 18059 Rostock, Germany

Introduction

In this study we report the application of ionic liquids (IL) for thermomorphic solvent systems (TMS) with upper critical solution temperature (UCST)-type behavior for an enzyme catalyzed reaction.

Thermomorphic solvent systems consist of solvent mixtures that exhibit a temperature-dependent miscibility gap, which allows a reversible macroscopic phase change between mono- and multiphasic conditions by a simple change of temperature (Figure 1). This effect can be used to improve productivity of a catalytic reaction and simplify downstream processing.[1]

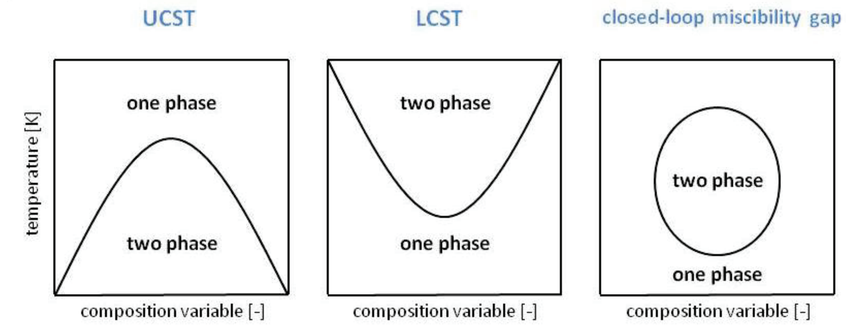
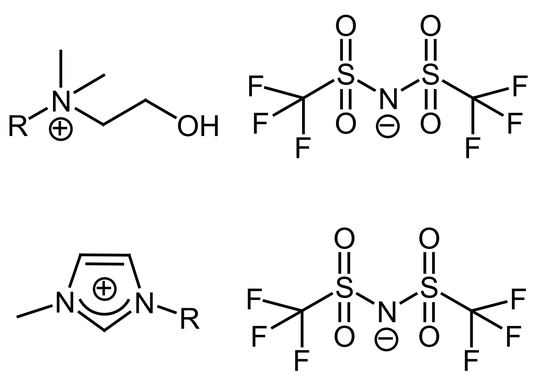


Figure 1. Phase diagrams of thermomorphic solvent systems; UCST - upper critical solution temperature, LCST - lower critical solution temperature

Results

Ionic liquids-based thermomorphic systems

A selection of choline- and immidazolium-based ionic liquids and MTBE (as a reference) were evaluated regarding their UCST phase behavior (Figure 2). Especially choline-based ionic liquids provided applicable solvent mixtures with an upper critical solution temperature (UCST) close to the temperature optimum of the enzyme (Table 1).[2]



Abbreviations

$[N_{1112}(OH)][NTf_2]$ - R=CH_3
$[N_{1122}(OH)][NTf_2]$ - R=C_2H_5
$[N_{1132}(OH)][NTf_2]$ - R=*n*-C_3H_7
$[N_{1142}(OH)][NTf_2]$ - R=*n*-C_4H_9
$[N_{1152}(OH)][NTf_2]$ - R=*n*-C_5H_{11}

$[EMIM][NTf_2]$ - R=C_2H_5
$[BMIM][NTf_2]$ - R=*n*-C_4H_9

Figure 2. Investigated ionic liquids that facilitate UCST-behavior with additional solvents

Several thermomorphic solvent systems with cloud point temperatures between 25 and 70 °C were identified and characterized for the intended enzyme catalyzed reaction (selected results in table 1). Lower values can be achieved by addition of an additional co-solvent such as 2-propanol and 1,4-dioxane.

Table 1. Thermomorphic solvent systems with a UCST between 25 and 70 °C (selected results for representation)

no	ionic liquid	secondary solvent	co-solvent	Temp.
1	0.25 g $[N_{1112}(OH)][NTf_2]$	750 µl 50 mM KPi-buffer	-	62 °C
2	0.30 g $[N_{1112}(OH)][NTf_2]$	700 µl 50 mM KPi-buffer	100 µl 2-propanol	38 °C
3	0.20 g $[N_{1112}(OH)][NTf_2]$	800 µl 50 mM KPi-buffer	100 µl 1,4-dioxane	50 °C
4	0.20 g $[N_{1112}(OH)][NTf_2]$	800 µl 50 mM KPi-buffer	100 µl acetonitrile	70 °C
5	0.30 g $[N_{1112}(OH)][NTf_2]$	300 µl MTBE	50 µl 2-propanol	25 °C
6	0.30 g $[N_{1142}(OH)][NTf_2]$	500 µl 1-octanol	-	46 °C
7	300 µl $[EMIM][NTf_2]$	600 µl 1-octanol	-	35 °C
8	400 µl $[EMIM][NTf_2]$	300 µl 50 mM KPi-buffer	300 µl DMSO	35 °C
9	100 µl $[EMIM][NTf_2]$	400 µl 50 mM KPi-buffer	500 µl acetonitrile	50 °C
10	200 µl $[BMIM][NTf_2]$	200 µl 1-pentanol	-	40 °C
11	200 µl $[BMIM][NTf_2]$	200 µl 1-octanol	-	50 °C
12	75 µl MTBE	400 µl 50 mM KPi-buffer	300 µl acetonitrile	35 °C

Enzymatic conversion in UCST-systems

The most promising thermomorphic solvent system ($[N_{1112}(OH)][NTf_2]$, KPi-buffer and 1,4-dioxane) was used for the CalB (Lipase B from *Candida antarctica*)-catalyzed enantioselective hydrolysis of racemic 1-phenylethyl acetate (Figure 3).

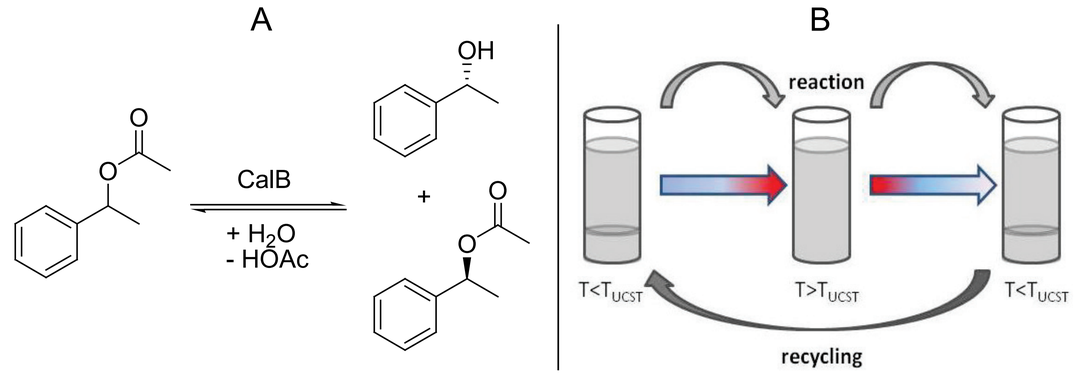


Figure 3. A) Enzymatic hydrolysis of (*rac*)-1-phenylethyl acetate, B) process concept utilizing the phase change of the thermomorphic solvent system

The investigated IL-based thermomorphic solvent shows a significant faster conversion than a organic solvent-based alternative (with MTBE) and a classical organic solvent. High enantiomeric excess of >99.5% was achieved for (*R*)-1-phenylethanol.[3]

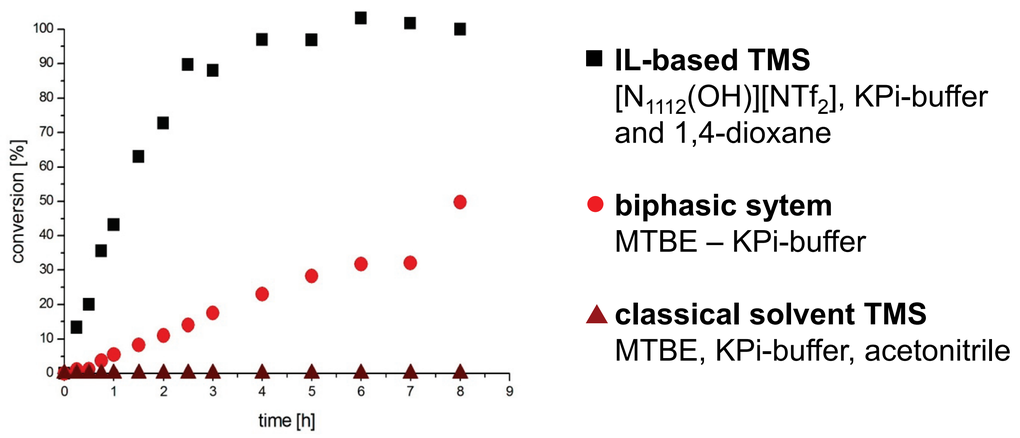


Figure 4. Comparison of the enzyme catalyzed hydrolysis in two thermomorphic solvent systems and a classical biphasic system

Summary

- Choline- and imidazolium based ionic liquids were investigated for the use in thermomorphic solvent systems.
- Cloud point temperatures between 25 and 70 °C were found.
- The IL-based thermomorphic solvent systems facilitates a considerable faster conversion.

References

[1] A. Behr, G. Henze, R. Schomäcker; *Adv. Synth. Catal.* **2006**, 348, 1485−1495

[2] A.J.L. Costa, M.R.C. Soromenho, K. Shimizu, I.M. Marrucho, J.M.S.S. Esperança, J.N.C. Lopes, L.P.N. Rebelo; *J. Phys. Chem. B* **2012**, 116, 9186−9195

[3] A. Gummesson, J. von Langermann, U. Kragl 'Biocatalytic Hydrolysis of Chiral Esters in Aqueous Ionic Liquid based Thermomorphic Solvents'; *manuscript in preparation*

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