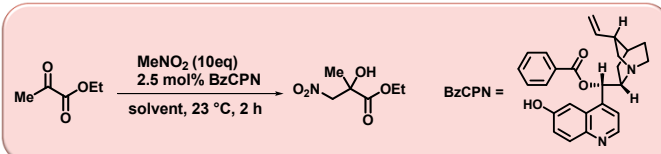


# Innovative Approaches for Catalyst Recycling in Organocatalysis

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## Introduction

The demand for sustainable, efficient and reliable methods for obtaining enantiomerically pure compounds as precursors in the pharmaceutically industry is steadily increasing. In addition to bio- and organometallic catalysed processes, organocatalysis gained a considerable impact in the past decades. However, a significant disadvantage of organocatalysis is still the requirement of high catalyst loadings (1-30 mol%) to achieve high selectivities and productivities. To overcome this drawback this study aims at three efficient catalyst recycling concepts.



Scheme 1. Benzoylcupreine-based organocatalyzed HENRY reaction.

## Results & Discussion

### Organic Solvent Nanofiltration<sup>[1]</sup>

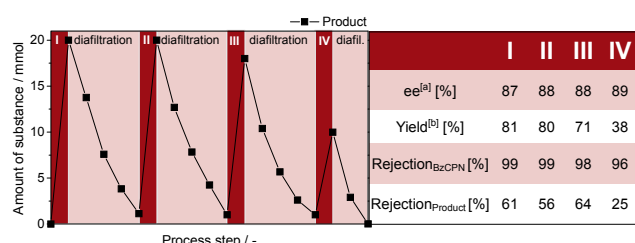


Figure 1. Amounts of product in the filtration cell during different reaction batches and diafiltration steps (I-IV denote the reaction batches). Cond. 25 mmol ethyl pyruvate, 10 mol% BzCPN, 10 eq MeNO<sub>2</sub>. <sup>[a]</sup>Determined by HPLC measurements. <sup>[b]</sup>Isolated yield after diafiltration steps and solvent removal.

### Poly(ionic liquid)s-based Immobilization<sup>[2]</sup>

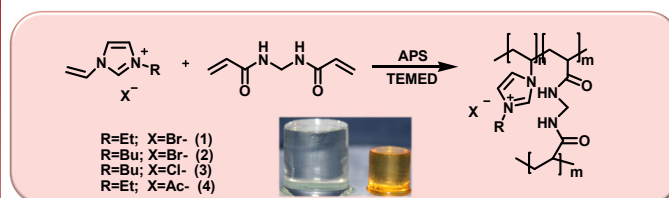


Figure 3. Preparation of poly(ionic liquid)s-based immobilization: Radical polymerization of an imidazolium-based ionic liquid bearing a vinyl group and cross-linker *N,N'*-methylenebisacrylamide, APS – Ammonium peroxydisulphate, TEMED – *N,N,N',N'*-Tetramethylethane-1,2-diaminediether.

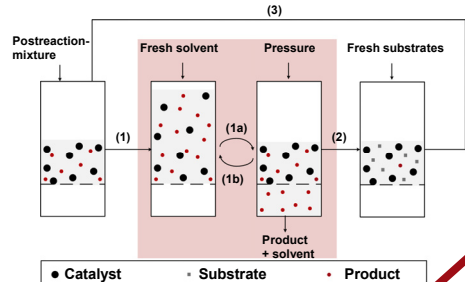


Figure 2. Process scheme for the diafiltration / reaction cycle in the stirred filtration cell: (step 1) discontinuous diafiltration of the diluted postreaction mixture; (step 1a) repeated filtration; (step 2) addition of fresh substrates; (step 3) subsequent reaction.

## Switchable-Hydrophilicity Solvents

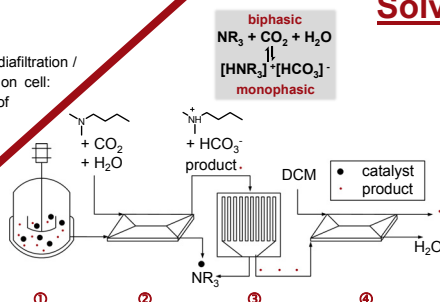


Figure 5. Instrumental setup for separation and recycling of organocatalyst by SHS. ① postreaction mixture, ② microextractor, ③ falling film microreactor, ④ microextractor.

BzCPN	
Soluble catalyst	90% ee <sup>[a]</sup> 90% yield <sup>[b]</sup>
Air dried (10 days)	61% ee 60% yield
Vacuum dried (10 days)	91% ee 62% yield
Solvent exchange	30% ee 20% yield

Figure 4. Catalyst activity with different drying methods. <sup>[a]</sup> 1 M ethyl pyruvate, 10 equiv. of MeNO<sub>2</sub>, 2.5 mol% cat. in PILs, 12 h, 23 °C. Hydrogels were dried on air / under vacuum for 7 days. <sup>[b]</sup> Determined by HPLC measurements.

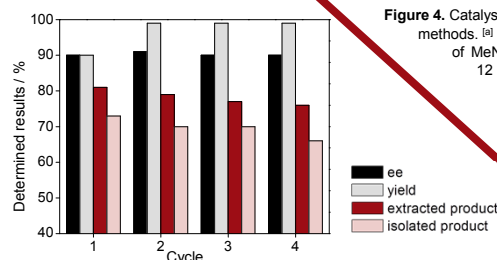


Figure 6. Results for recycling experiments. Conditions: 10 mL postreaction mixture (in EtOAc), 0.1 M product, 2.5 mM catalyst, 10 mL SHS (1e),  $\Phi$  = 25 °C, phase ratio 1:1, FFMR for removing CO<sub>2</sub>,  $c_{cat}$  was determined by UV/Vis,  $c_{prod}$  was determined by HPLC.

## Summary

Table 1. Comparison of the three approaches for catalyst recycling in organocatalysis.

	OSN	PILs	SHS
Catalyst loading / mol%	10	2.5	2.5
Substrate amount / mmol	25	10	10
Enantioselectivity / %	89	88	91
Yield / %	81	62	99
Recycling Number	4	4	4
TON	27	58	156

We illustrate three innovative approaches as an alternative separation technology to existing methods. OSN is particularly attractive for subsequent industrial processes since no immobilization, no additional additives or additional energy consumption is required. The embedding of organocatalysts in IL-based hydrogels offers a simplified downstream processing of the product to a large extent. With a wide range of tertiary amines, SHS can be finely tuned to catalysts and products with different hydrophobicities. These techniques will open a new window in organocatalysis for the production of chiral building blocks on an industrial scale.

