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Process considerations and economic evaluation of biocatalytic production of chiral amines using transaminases

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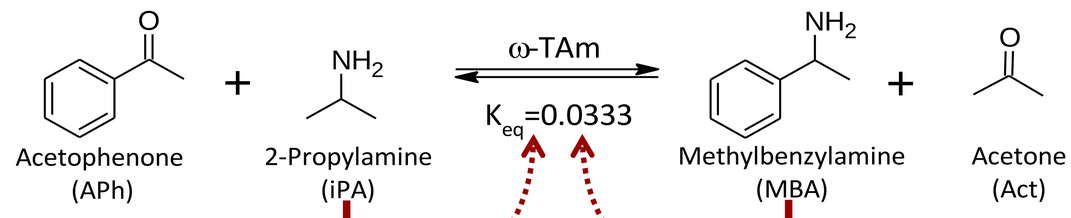
Introduction

•Asymmetric synthesis of chiral amines can be achieved by transaminase catalyzed reactions. These catalysts can transfer an amine group from an amine donor (AD) to a pro-chiral acceptor ketone (Ket), yielding a chiral amine (ChA) with simultaneous production of a ketone as co-product (CoP).

• Despite the recent publications reporting high catalyst productivities and product concentrations [1-3], there are several challenges that need to be overcome in order to make transaminase processes competitive for a wider range of amines (e.g. reaction thermodynamics, and catalyst kinetics). Different solutions might successfully overcome the process challenges [4].

• This work assesses the different process solutions and their economic profile.



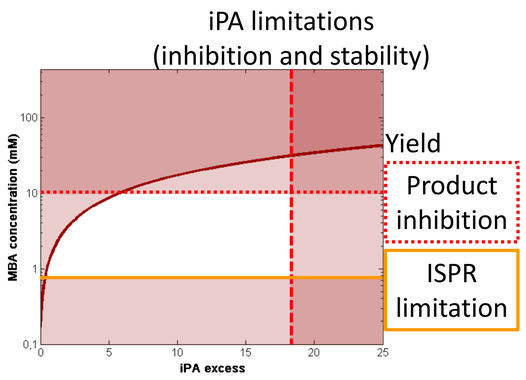


Figure 1 – Thermodynamic operating windows for MBA production using ISPR and amine donor (iPA) excess to shift equilibrium. Aim: 90% yield.

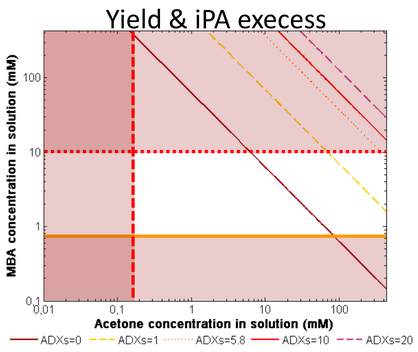


Figure 2 – Thermodynamic operating windows for MBA production using ISPR, amine donor (iPA) excess, and *in-situ* co-product (acetone) removal to shift equilibrium. Aim: 90% yield.

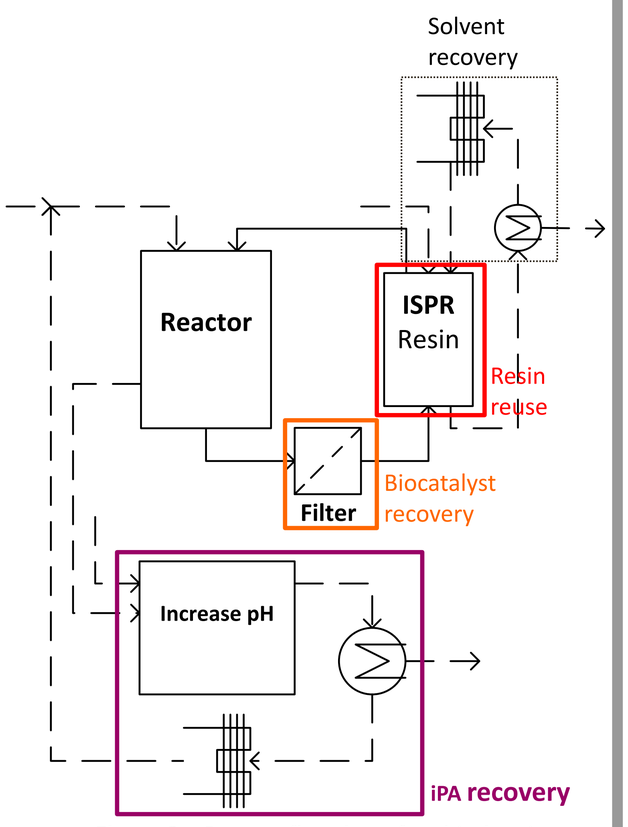
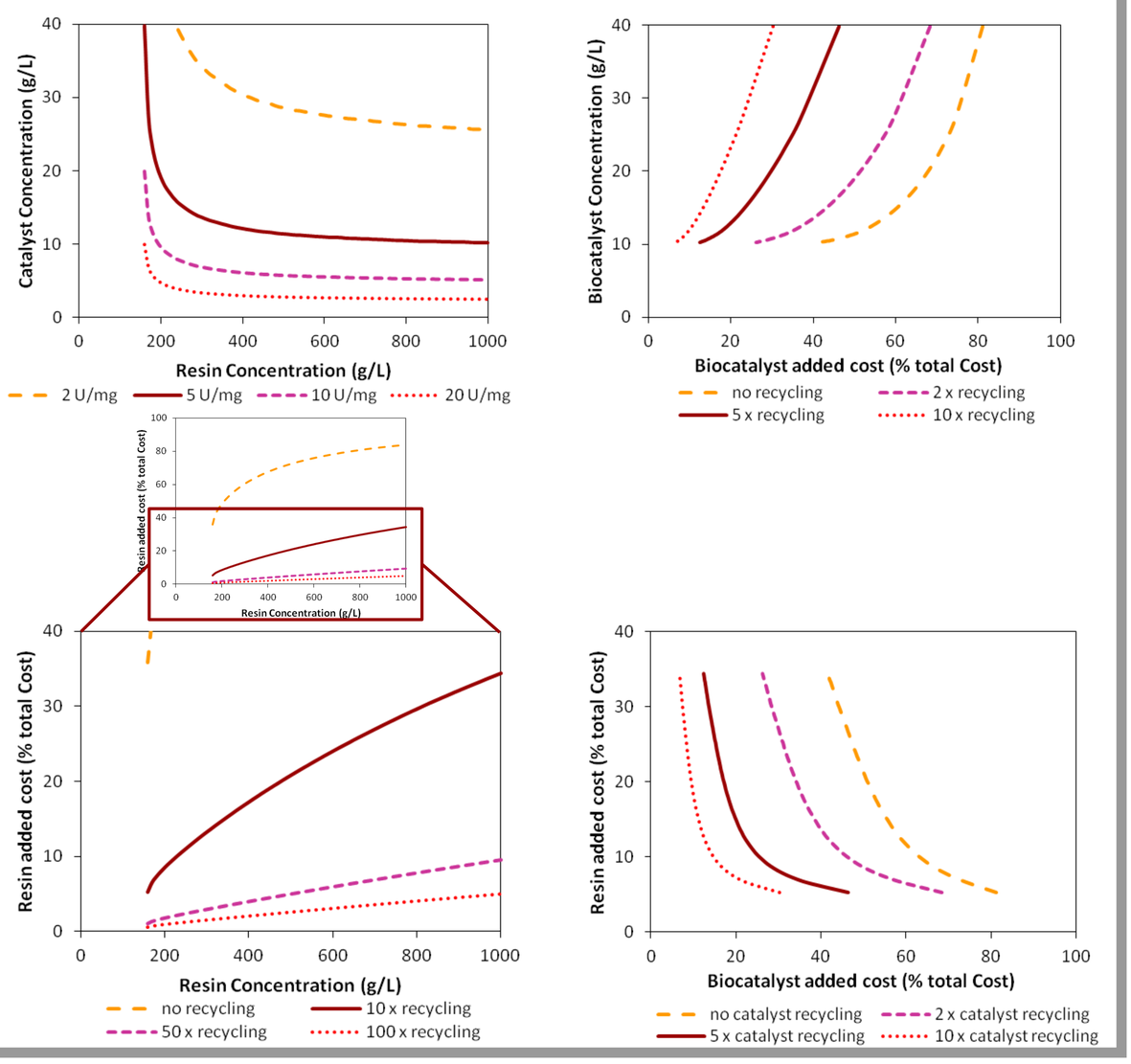
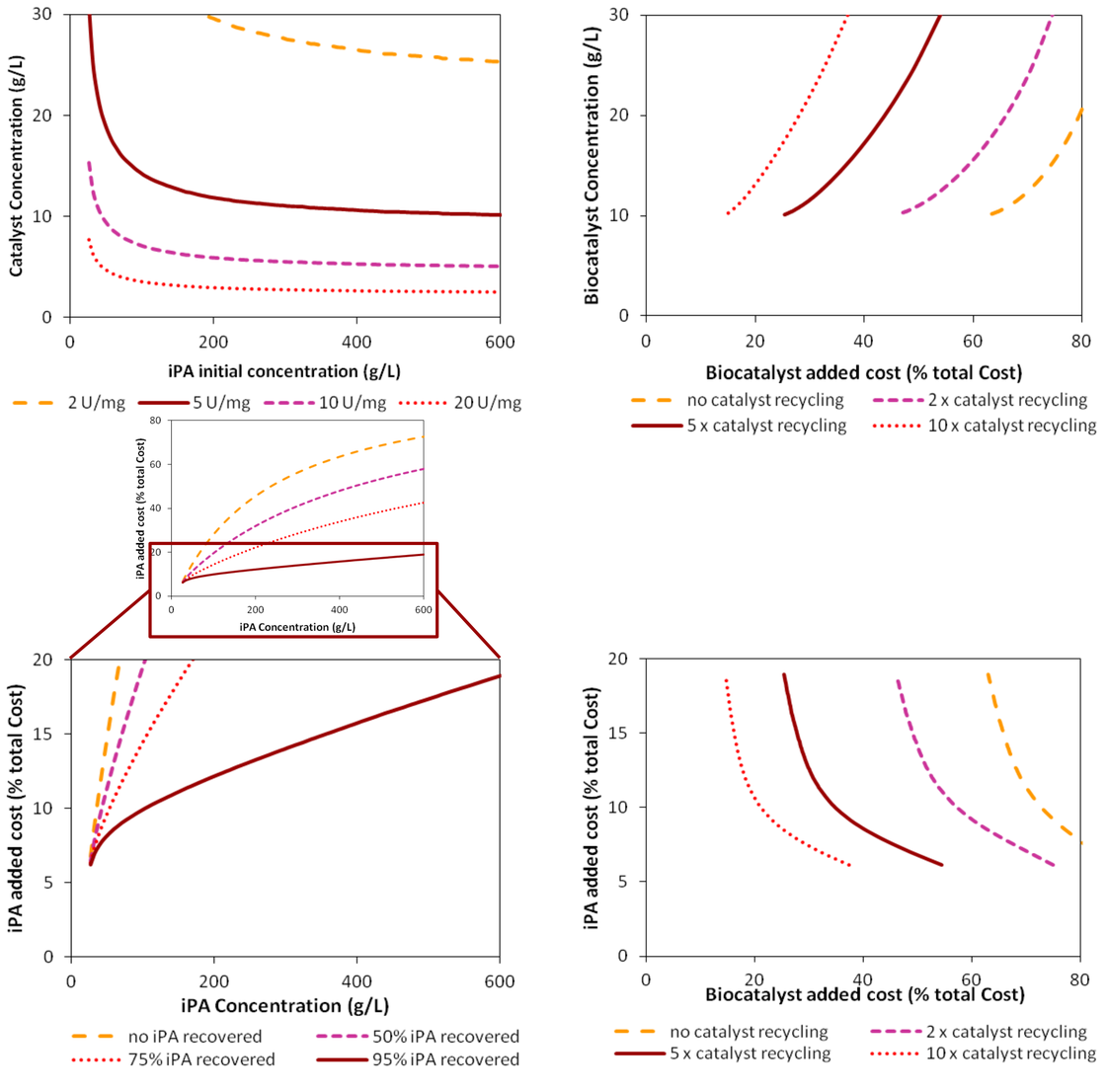


Figure 3 – Process flowsheet for chiral amine production

In-situ Product Removal



Amine Donor Excess



Conclusion

• Resin and catalyst recyclability, and amine donor recovery, have a strong impact on the process economic profile, with a sharp added cost increase when these options are disregarded.

• There is trade off between the catalyst activity (i.e. quantity of catalyst needed) and product concentration, here expressed as ISPR required (i.e. amount of resin required).

• The effect of the amine donor excess on the catalyst activity seems to be related, primarily with the reaction thermodynamics, as the catalyst activity is not highly affected when iPA concentration increases. However, for lower values of amine donor excess, the increase in concentration relates with a increase on the catalyst activity (i.e. lower catalyst concentrations).

References & Acknowledgements

[1] Martin *et al.* 2007. Biochem Eng J 37: 246-255
[2] Truppo *et al.* 2010. Org Proc Res Dev 14:234-237
[3] Savile *et al.*2010. Science 329: 305-309
[4] Tufvesson *et al.* 2011. Biotech Bioeng 108 (7): 1479-1493.

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