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[C0001]

Substrate Transport Limitation as tool to enhance enantioselectivity in the enzyme synthesis of chiral cyanohydrins

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Objective

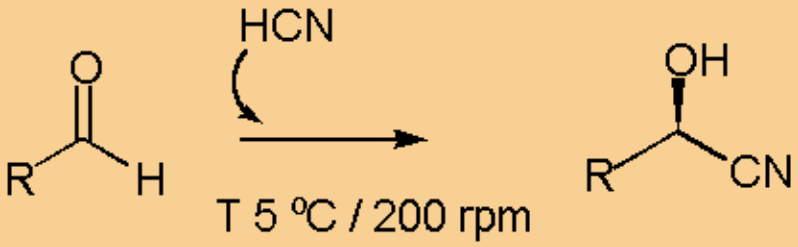
Rational design of process characterized by:

- two-phase (fed) batch system
- the use of purified oxynitrilase
- enantiomerically pure products (*ee* > 98%)
- high yield and through-put (mol.l^{-1}.h^{-1})
- down stream processing with respect to recycling of enzyme and solvents

Justification

- the almond enzyme is readily available at low cost
- the reaction products, chiral cyanohydrins

Experimental conditions



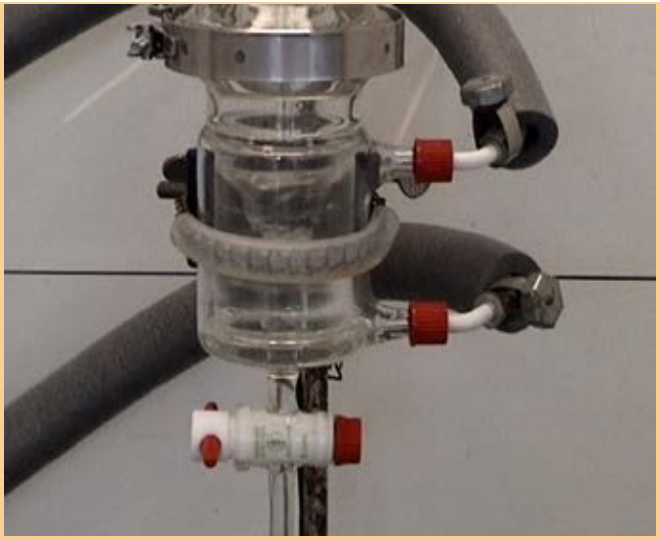


Figure 1. On the left the reaction scheme showing the general reaction. On the right the double-walled reaction vessel used in the here described synthesis (Copyright J.Marcus 1999)

Results

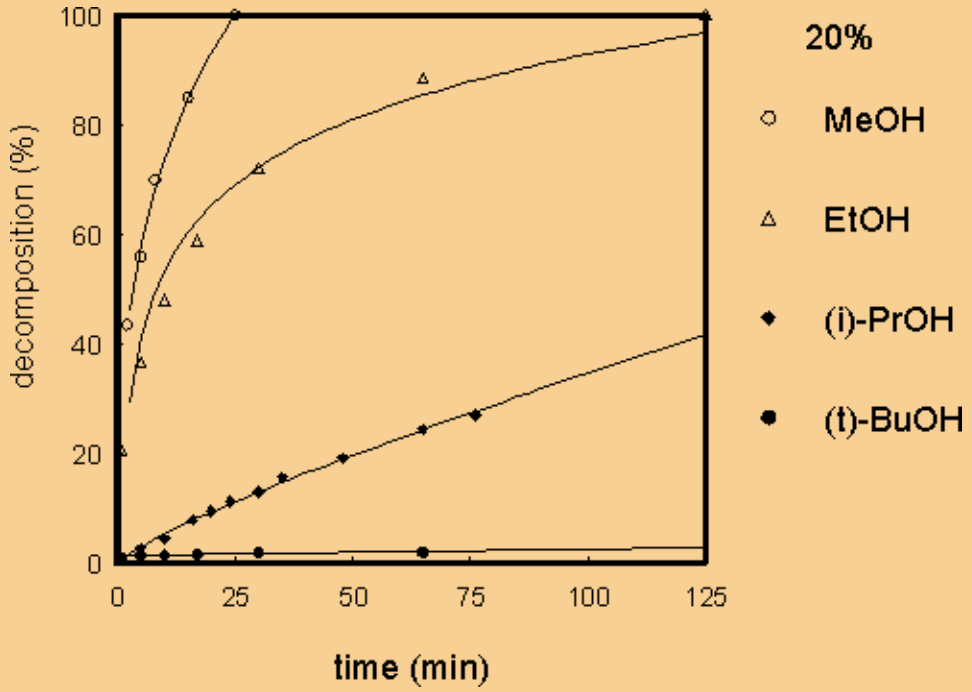


Figure 2. Effect of co-solvent on the stability of the cyanohydrin in hexane and proposed mechanism for the interaction of alcohols with cyanohydrins[1]

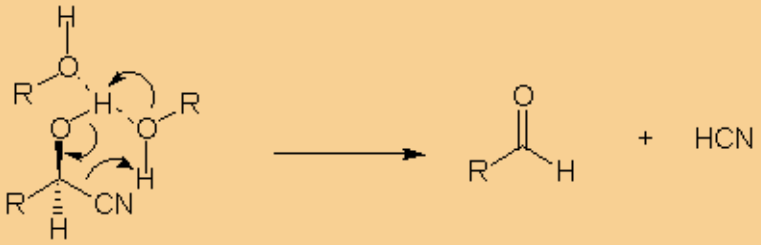


Figure 3. Proposed mechanism for the decomposition of cyanohydrins under influence of alcohols.

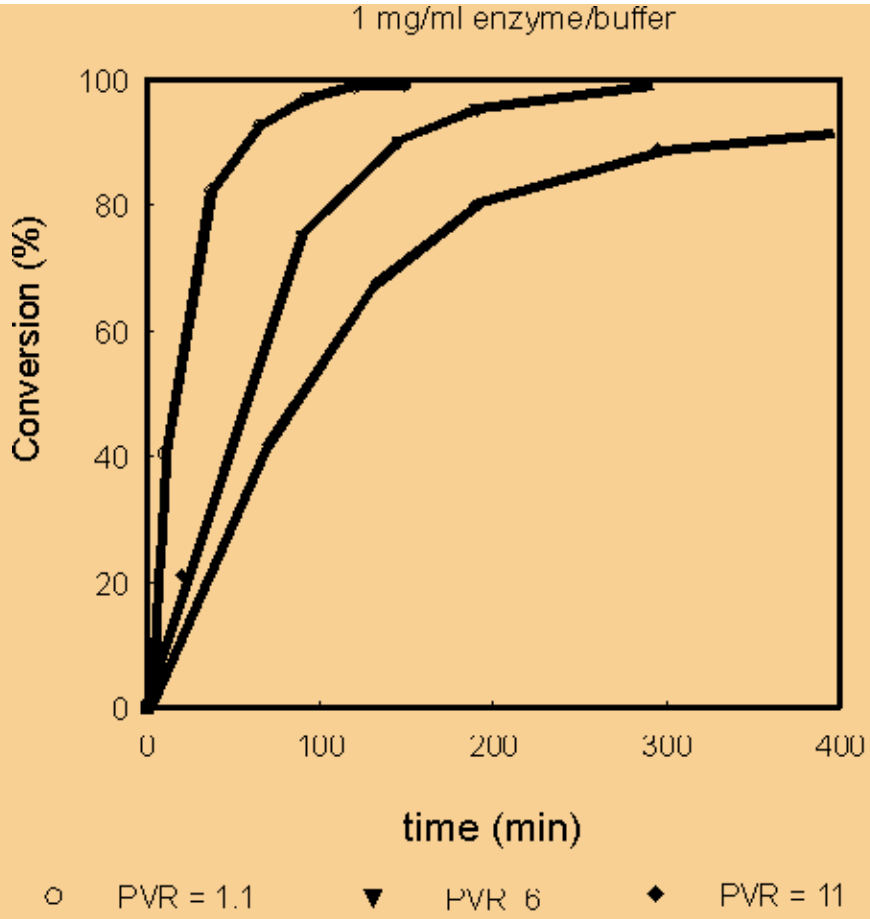


Figure 4. Varying the Phase Volume Ratio (PVR) and monitoring the reaction in time

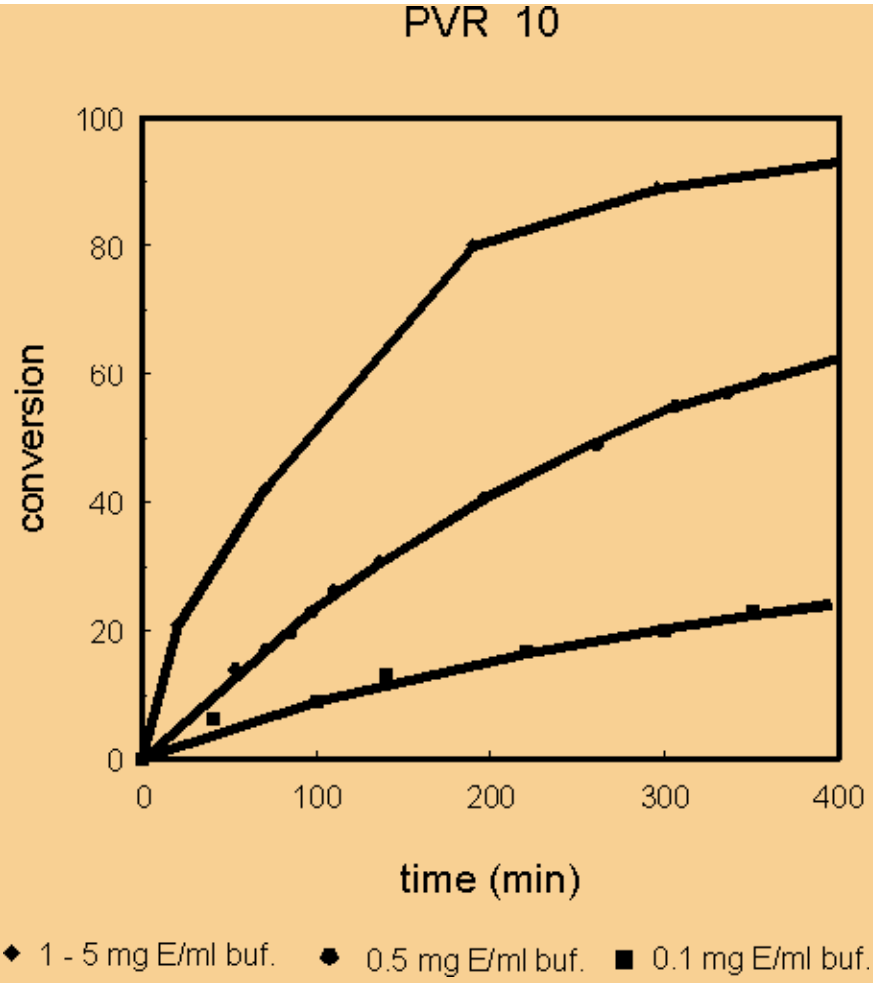


Figure 5. Varying the enzyme concentration (constant substrates concentration and PVR) and monitoring the reaction rate in time below reaction rate limited enzyme concentration

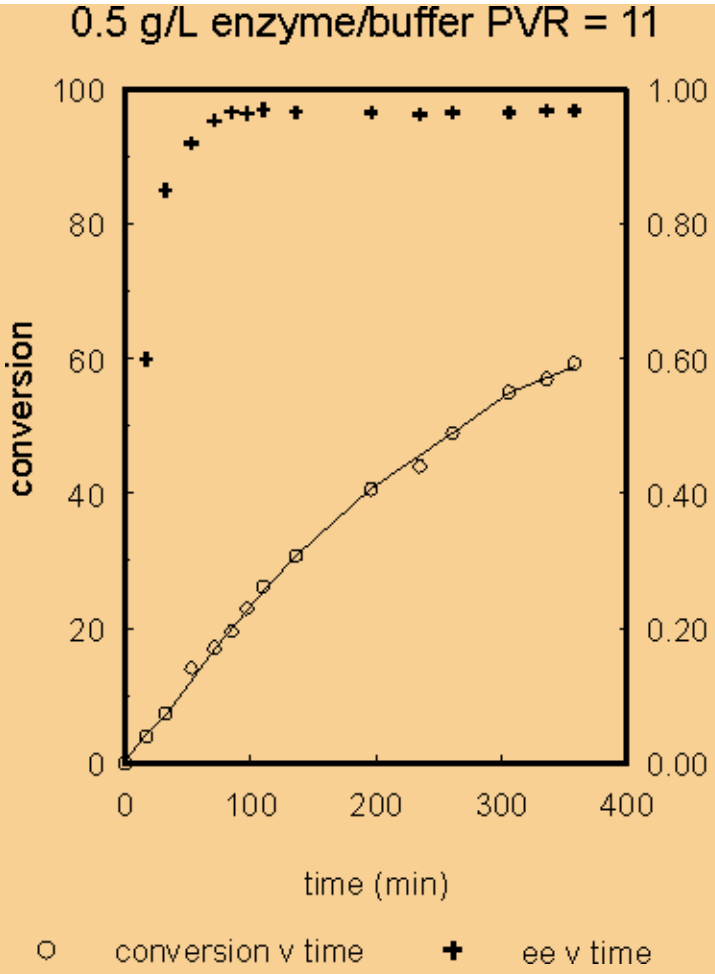


Figure 6. Influence of enzyme concentration on *ee* and reaction rate, reaching a steady state, below reaction rate limited enzyme concentration

Conclusions

- **Do not use alcohols as co-solvent: alcohols influence the stability of cyanohydrins, the kind of alcohol employed has an important effect on the decom-position rate.**
- **optimization of enzyme conditions can give good results even if the non-enzyme catalyzed reaction is favorite**
- **There exists a constant ratio between both reactions expressed in an enantioselectivity coefficient**
- **high PVR reduces reaction rates and enhances the enantioselectivity**
- **Substrate Transport Limitation is a powerful tool to enhance enantioselectivity in a two phase system**

Reference

[1]Marcus, J.; Vandermeulen, G.W.M.; Brussee, J.; van der Gen, A. *Tetrahedron: Asymmetry* 1999, *10,* 1617-1622.

More information about this subject and other projects of our group can be found on our homepage:
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