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Thermodynamic Evaluation of the Production of Chiral Amines from Long-Chain Aliphatic Alcohols

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Introduction

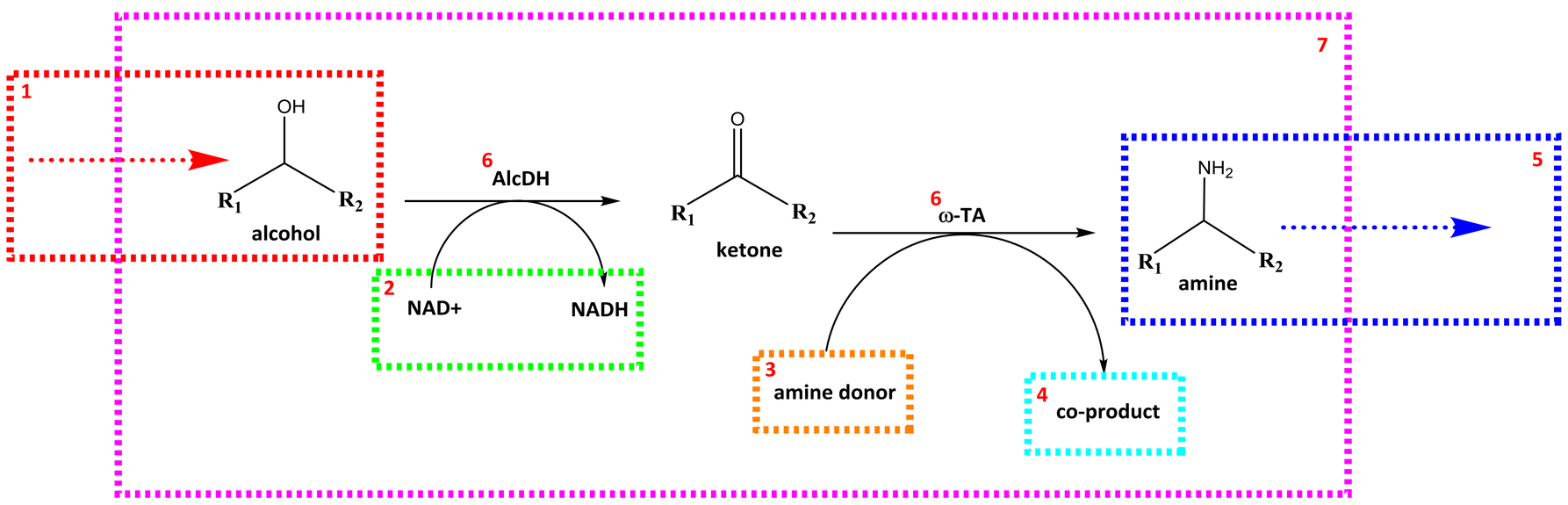
ω-Transaminase (EC.2.6.1.X) has been receiving considerable attention in chiral amine production due to its excellent stereoselectivity and its ability to operate under mild conditions. Potentially of even greater interest is to use alcohols as the starting material rather than ketones to produce the corresponding amines using a combination of an alcohol dehydrogenase (EC.1.1.1.2) in combination with the ω-transaminase [1, 2]. However of both reactions are reversible and often limited by thermodynamics where the equilibrium positions are in the favour of the reactants rather than the products.

Thermodynamics

Thermodynamic equilibrium of a system is very crucial it in large part responsible for determining the yield of the reaction. However, very little attention has been addressed on this issue in the scientific literature compared to the kinetic study of enzyme-catalysed reactions [3,4].

- For unfavourable reaction equilibrium, the reaction can be made possible and improved by shifting the equilibrium position towards the product with reaction process engineering and engineering strategies.
- For favourable reaction the study on kinetics will be useful and significant for control strategies.

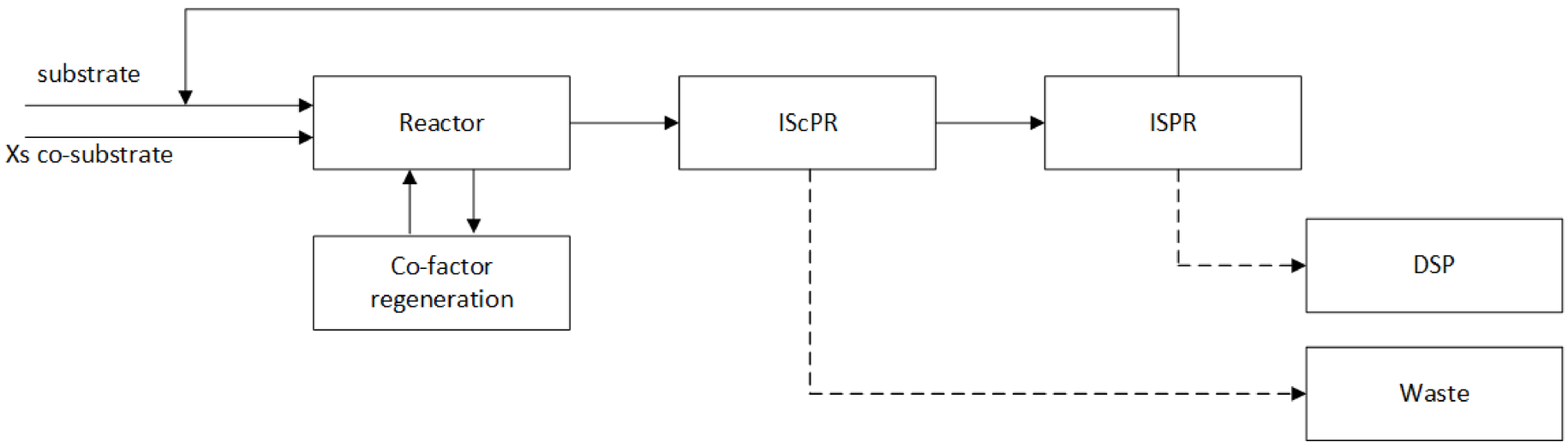
Process Challenges



Solutions:

1. Substrate feeding strategy
2. Co-factor regeneration or enzyme cascade
3. Excess of amine donor
4. *In-situ* co-product removal or enzyme cascade
5. *In-situ* product removal
6. Biocatalyst format & amount
7. Reactor configuration

Example Flowsheet



Thermodynamic estimation

- Experimental methodology to determine K_{eq} [3]

$$Q = \frac{[C][D]}{[A][B]} \xrightarrow{t=\infty} K$$

[A],[B],[C],[D] corresponds to reactant concentrations

$$\frac{Q_t}{Q_0} \rightarrow 1, when\ Q \sim K$$

- Predictive tools to calculate of ΔG value using group contribution method [5, 6]

Process Perspective

There is a need to predict the thermodynamic equilibrium value of the system in order to guide decision making and to set a realistic target for scale-up.

The engineering tools used to assist process development

- Thermodynamic modelling
- Kinetic modeling

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