

- We can now rapidly evolve / produce enzymes that are productive process catalysts.
- Enzymes can be evolved/developed starting from zero activity.
- *In silico* modelling and understanding enzyme structure and function can provide insight for engineering.
- Enzymes can be developed to operate in harsh chemical environments never found in nature.
- The mild conditions and high selectivity of enzyme transformations can give more productive processes – often in perfect ee for chiral compounds.
- Biocatalytic processes can give shorter and more streamlined manufacturing processes when compared to their chemical equivalents.
- Biocatalysts can replace expensive/rare metal catalysts.

- Developing a productive process with a biocatalyst is not too different to using a metal / chemo catalyst.
- We need to consider (bio)catalyst stability and productivity at relevant industrial concentrations.
- Productivity can suffer from substrate/product inhibition – this is also true for metal / chemo catalysed reactions as well.
- Understanding the mechanism of enzyme inhibition/inactivation is key to solving the problem.
- Understanding the structure/activity of the enzyme is vital to fast and efficient optimisation via mutagenesis.
- A lot can be achieved through in silico modelling.

We have seen that the KRED enzyme class can be used in chemical processes

- to manufacture chiral alcohols.
- Many companies now look to KREDS as a primary route to chiral alcohols
- Enzymes can be evolved to work with very 'unnatural substrates (at acceptable rates).
- Do not always require high solubility of substrate
- KRED'S totally selective for ketone in the presence of other reducible functionality

The use of KRED enzymes can give processes that:

- Use less material
- Use less organic solvent
- Replace undesirable chemical reagents
- May be more sustainable than other alternatives
- Can utilise isopropanol oxidation to drive co-factor recycle



We have seen in this example that biocatalysis can be used in chemical processes for bulk chemicals (monomers).

The nitrile hydratase process has shown that:

- Biocatalysis is not applicable to only chiral products
- Biocatalysis is not just applicable to low volume, high value products
- Enzymes can be developed to operate in harsh chemical environments
- The mild conditions and high selectivity of enzyme transformations can give more productive processes with sensitive / highly reactive substrates.
- Biocatalytic processes can give shorter and more streamlined manufacturing processes when compared to their chemical equivalents
- Toxic metal catalysts / corrosive reagents can be replaced by a biocatalyst
- Biocatalytic processes can have lower energy demand
- Enzyme-mediated strategies can be more sustainable than their alternatives

In this case study of the production of 7-ACA, we have seen:

- Different enzyme be linked and used in a manufacturing process.
- Enzymes supported on a matrix, bringing benefits to the process.
- Oxidation chemistry without metal catalysts, with air, under mild conditions.
- A process operating nearer ambient than cryogenic temperature brings big energy savings - biocatalysis can allow this in some cases.

As with chemical catalysts, the following are required:

- Careful definition of operating conditions in order to maximise catalyst stability.
- Consideration mass transport of gas phase reagents into the reaction mixture.