CatSci
BEYOND PROCESS CHEMISTRY

Opinion Piece

WHY BIOCATALYSIS

By Dr Andy Wells, CatSci's biocatalysis expert

A TOUGH START

Enzymes are nature's catalysts. They have evolved to grow and maintain the processes that's support life. More than 30 years ago when I first read a journal article describing the use of enzymes as catalysts in an organic synthesis I was inquisitive, amazed but also sceptical. I recall thinking at that time, will this ever be a widely accepted and used part of the synthetic chemist's tool box, or will we just see the odd example as more of a scientific curiosity. At that time, many thought the latter, with the issues listed below being seen as major impediments:

- Esoteric – not many enzymes available
- Small scale – milligrams of substrate
- High cost and lack of availability
- Need microbiology/fermentation expertise
- Enzymes do not accept unnatural substrates
- Cannot be used with organic solvents
- Need very dilute reactions
- Driving co-factor recycling with redox enzymes/cost of co-factors
- Equilibrium reactions inherently resulting in incomplete conversion

INDUSTRIAL RECOGNITION

Fortunately, over the ensuing decades, the explosion of understanding of molecular biology, modern techniques to understand protein structure and function, greater accessibility of DNA sequencing and synthesis, and the ability to rapidly evolve bespoke task-specific enzymes has overcome most of these issues and made biocatalysis available to all willing to invest time to develop and build expertise in house or collaborate with partners with existing expertise and networks in the field.

Alongside the topic of biocatalysis, most synthetic organic chemists think of the production of chiral molecules and indeed, many enzymes with their exquisite stereoselectivity are ideally suited for this mission. But biocatalysis can bring so much more to assist the chemist in designing novel, safe and sustainable routes to commercial target molecules:

- ✓ Highly stereo-, chemo- and regio-selective reactions with multi-functional substrates
- ✓ Functional group conversion and carbon-carbon bond synthesis
- ✓ May access reactions/selectivity that are difficult or impossible via traditional chemical catalysis/synthesis
- ✓ Efficiency – potential for very high turnover numbers
- ✓ Economics – simple whole cell reactions, or recovery and re-use of a supported, isolated enzyme
- ✓ Will catalyse reactions under mild conditions – can use sensitive substrates
- ✓ Work near ambient temperature, atmospheric pressure and pH 7
- ✓ Potential for clean/green processes

SO, IS A BIOCATALYTIC ROUTE ALWAYS THE BEST?

Of course, this is not always the case, but biocatalysis has now been established as an essential part of the synthetic chemistry tool box and more examples are appearing on a regular basis where biocatalysis is the key enabling technology to access a range of molecules for research purposes, part of a tactical route to deliver initial supplies of material, or as part of a more strategic long-term manufacturing route.

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RECENT ADVANCES

Biocatalysis/industrial biotechnology is a rapidly expanding field and maintaining awareness around new developments is crucial. A couple of recently published papers that I have enjoyed reading:

- **Application of ω-Transaminases in the Pharmaceutical Industry; Chem. Rev. 2018, 118, 349−367.** The synthesis of chiral amines using biocatalysis has become a crucial part of the synthesis toolbox. This timely and comprehensive review demonstrates what can be achieved with the ω-Transaminases enzyme class.
- **Artificial Biocatalytic Linear Cascades for Preparation of Organic Molecules; Chem. Rev. 2018, 118, 270−348.** An area of intense interest – linking multiple enzyme catalysed reactions to take simple building blocks to complex intermediates. A few scaled examples exist already, many more will undoubtedly be developed in the next few years. Kroutil *et al.* have reviewed a decade of progress in this area.

FREE COURSES

Finally, if you are an interested/curious non-practitioner and would like to learn more about biocatalysis and industrial biotechnology in general, and how this technology can be used in industrial processes with a clear focus on why the bio-manufacturing route was chosen over more traditional chemical processes, I can recommend:

- the CHEM21 learning platform: http://learning.chem21.eu/
- the University of Manchester Massive Online Open Course: https://www.coursera.org/learn/industrial-biotech

Both courses are free to use and are designed and targeted at the non-expert user.

Dr Andy Wells is CatSci's in-house biocatalysis expert. He is a specialist and expert in the field of chemical process R&D where, over the past 30 years, he has spent most of his professional career employed at three multi-national pharmaceutical companies, rising to the rank of Senior Principal Scientist (Director Level) at AstraZeneca. His career has spanned across a broad range of scientific disciplines, and he is a keen exponent of working at the interface of the physical and biological sciences to champion the adoption of novel, more sustainable technologies across a range of business areas.

Want to find out more?
Visit our website to take a look at our Case Study on Biocatalysis

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