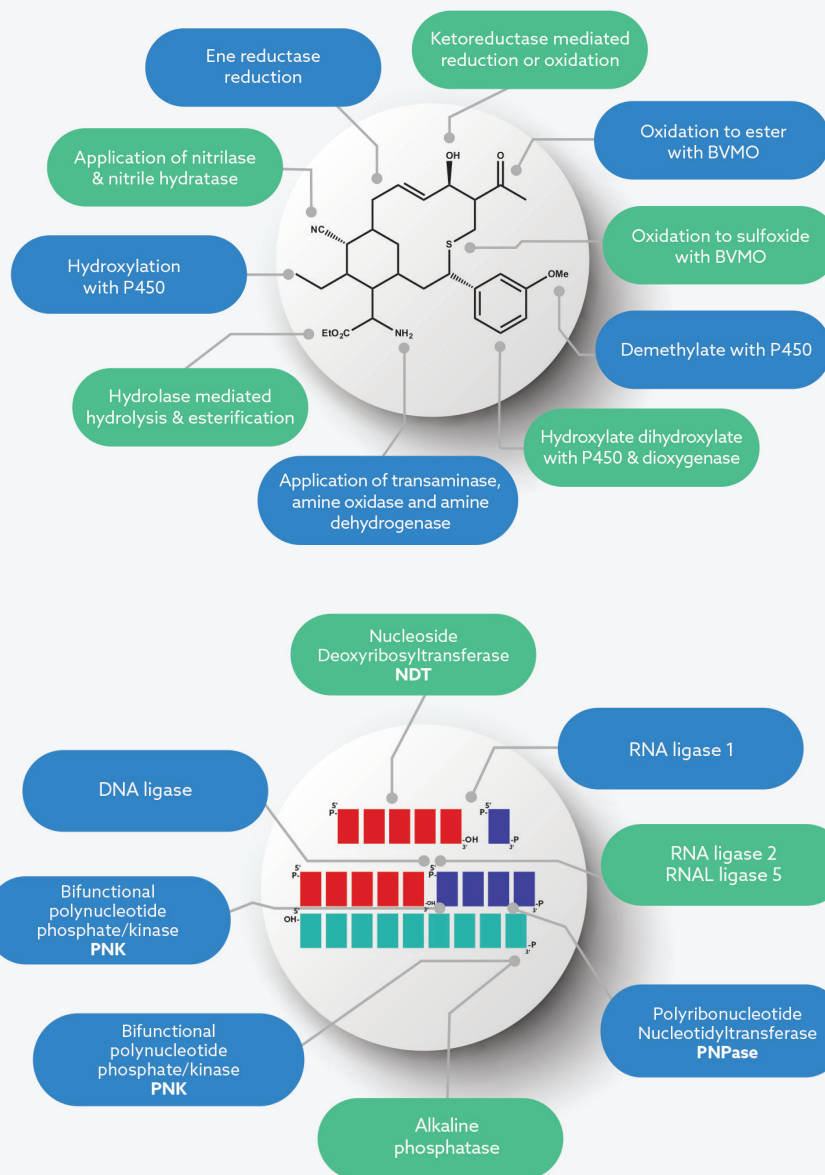


selectAZyme™

- **selectAZyme™** is Almac's technology platform of recombinant enzyme libraries
- Integrated group of biologists, computational and process chemists
- Supply and screening of enzyme libraries
- Biotransformation and DSP development supported by chemical processing expertise
- Fermentation development and scale-up
- Enzyme formulation development and manufacture
- Metabolite synthesis, isolation and structural identification
- Gram to tonne manufacture of intermediates and active ingredients





selectAZyme™

Almac's biocatalysis expertise ranges from enzyme discovery, enzyme engineering and enzyme production to the synthesis of complex chiral intermediates and active ingredients, all based on selectAZyme™ technology. Challenge us with your chemistry problems and see how we can successfully deliver biocatalysis solutions and more...

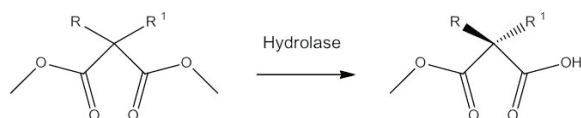
Almac has invested significantly in this area to develop robust enzymes with improved properties for chemical manufacturing.

We offer the following:

- Screening of our biocatalyst toolbox with customer substrates
- Biocatalytic route design and process development
- Enzyme supply on a price per kilogram or activity basis
- Enzyme engineering and development of formulation and immobilisation
- Tech transfer and on-site support of manufacturing activities
- Supply of chiral RSMs, intermediates and APIs (cGMP and non-GMP)
- Metagenomic enzyme library generation
- Fermentation development and scale-up
- Metabolite synthesis
- FTE or FFS contracts

Case studies

Case study 1 - Desymmetrisation of diester using hydrolase enzymes

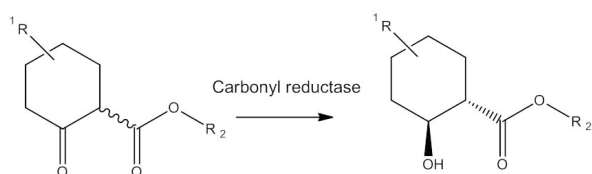


Client required development of a hydrolase mediated desymmetrisation process for tonne manufacture.

The Almac Solution involved:

- Enzyme screening and identification of L-44 enzyme
- Process optimisation and pilot scale demonstration
- Technology transfer back to customer site
- Enzyme supply to support manufacture

Case study 2 - 200 kg chiral intermediate supply

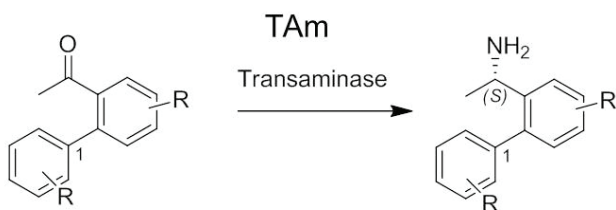


Client required supply of a chiral intermediate for chiral intermediate supply.

The Almac Solution involved:

- Replacement of a multi step route with a single dynamic bioreduction step
- Chemistry controlled to 91% yield, >99.0 % e.e. resp. d.e. with >98.5 % purity
- Enzyme screening identified CRED-A161 with GDH/glucose for cofactor recycling

Case study 3 - Chiral amine synthesis

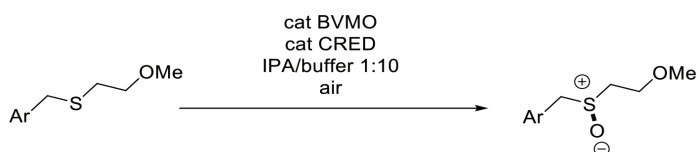


Client required novel technology solution for the multi-kg manufacture of a chiral amine.

The Almac Solution involved:

- Identification of development lead via transaminase library screening
- Enzyme engineering required to meet targeted product titre and enzyme loading
- KPIs reached with ~300 mutants computationally selected over two rounds

Case study 4 - BVMO process for chiral sulfoxide

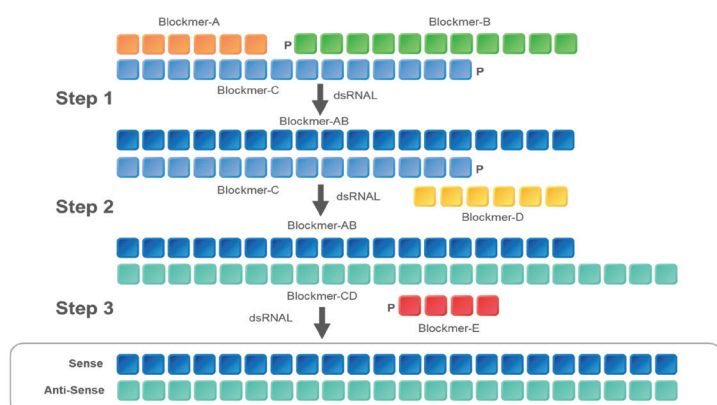


Client required development and GMP scale up of their bio-oxidation process.

The Almac Solution involved:

- Expression boosting the client supplied enzyme sequence
- Process optimisation for productive and safe scale up
- Several cGMP batches in 1,000 L reactor, delivering 30 g/L product

Case study 5 - Enzymatic synthesis of double-stranded RNA (dsRNA)



Client requested a biocatalytic route for synthesising a dsRNA featuring distinct 2'-substituents.

To achieve this goal, Almac's 3-2-3-2 hybrid Biocatalytic Oligonucleotide Synthesis Technology (BOOST) was employed:

- PNK enzymes phosphorylate 5' end of blockmers prior to ligation
- 3 blockmers were annealed followed by ligation to form 2 RNA pieces
- Sequential addition of blockmers with annealing and ligation was repeated to form target duplex
- This technique allowed favourable base pairing and ligation points to be selected for small oligonucleotide blockmers

RNA ligase and PNK enzymes were initially discovered and subsequently engineered through rational design, site-saturation mutagenesis, and directed evolution to fulfill the client's requirements for specific blockmers and the final dsRNA product.

Our capabilities and expertise

Almac's technology platform can be applied throughout your product lifecycle to guide synthesis projects from conception to scale-up.

Research

- Rational enzyme discovery and engineering
- INSIGHT metagenomics enzyme discovery
- Machine learning assisted enzyme discovery and engineering
- Enzyme selection via directed evolution
- Strain and pathway engineering
- New route design and consultancy

Process intensification and manufacture

- Enzyme immobilisation for faster reaction and simple DSP
- Ultrasound assisted biotransformation technology
- Integration of biocatalysis and flow chemistry steps
- Bulk enzyme supply
- Chiral building block and RSM supply
- GMP manufacture of APIs and intermediates

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