BIOTRANS
LA ROCHELLE 2023

N°498 /
TOPIC(s) : Industrial biocatalysis / Biocatalytic cascade reactions

Biocatalytic hydrogenation: robust biotechnologies for sustainable chemical manufacturing

AUTHORS
Holly REEVE / HYDREGEN, CENTRE FOR INNOVATION AND ENTERPRISE, OXFORD
Sarah CLEARY / HYDREGEN, CENTRE FOR INNOVATION AND ENTERPRISE, OXFORD

PURPOSE OF THE ABSTRACT

The use of enzymes as tools in chemical synthesis is growing thanks to technological breakthroughs, such as enzyme engineering and developments toward scalability. These advances make biocatalysis useful for a range of applications, from early stage drug discovery to chemical manufacturing. HydRegen's “black powder” biocatalytic hydrogenation systems, which are composed of enzymes immobilized on a carbon material, make biocatalysis simple to implement in chemistry settings due to similar catalyst handling to that of commonplace hydrogenation catalysts (e.g. Pd/C). The biocatalyst systems are powered by atom economical H2 gas, thus swapping out waste-intensive reductants that the enzymes typically rely on (e.g. glucose) while still taking advantage of the enzyme properties (mild operating conditions, excellent selectivity and functional group tolerance).

The HydRegen biocatalytic hydrogenation tools are useful across a range of applications: from route scouting and building chemical libraries, through to bespoke chemical syntheses demonstrated in scalable batch and continuous reactors. Case examples involve the use of different NADH-dependent enzymes to achieve a variety of asymmetric hydrogenation of double bonds (carbonyl, alkene) and reductive aminations. More recently we developed a broad scope tool for mild nitro reductions to the corresponding amines. An array of specialty chemicals have been prepared, including at multi-gram scale (100%, >99.9% ee) with simple catalyst removal and chromatography-free purifications. Fed-batch and continuous flow reactions have shown working week catalyst stability (5 days, > 1 million catalyst turnovers). Overall, we find our biocatalytic hydrogenation systems provide several advantages: avoidance of precious metals, decarbonization of traditional biocatalysis, excellent selectivity, functional group tolerance, no catalyst deactivation by typical poisons (e.g. sulfur), and slotting-in to existing hydrogenation infrastructure.

FIGURES

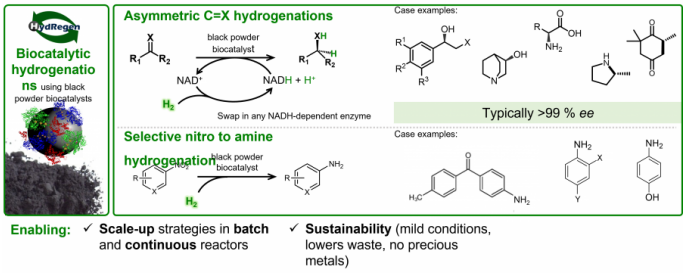

FIGURE 1

Heterogeneous biocatalysts enable mild and highly selective hydrogenations, from screening tools to scale-up strategies for sustainable chemical synthesis

Heterogenous biocatalysts for H2-powered NADH recycling coupled to asymmetric reductions, or nitro to amine conversions. Reactions proceed with excellent selectivity and allow operation of biocatalysis using standard chemical protocols.

FIGURE 2

KEYWORDS

biocatalytic hydrogenation | immobilised enzyme | continuous processes

BIBLIOGRAPHY

Reeve, H.A., Lauterbach, L., Lenz, O., Vincent, K.A. 'Enzyme-Modified Particles for Selective Bio-Catalytic Hydrogenation via H2-driven NADH Recycling' ChemCatChem, 2015, 7, 21, 3480-3487 DOI:10.1002/cctc.201500766

Cleary SE, Kazantzi S, Trenchard JA, Monedero M, Allman JW, Lurshay TC, Zhao X, Kenny MBC and Reeve HA (2023), Preparation of (3R)-quinuclidinol using heterogeneous biocatalytic hydrogenation in a dynamically-mixed continuous flow reactor. Front. Catal. 3:1114536. doi:10.3389/fctls.2023.1114536