Biocatalysis as Key to Sustainable Industrial Chemistry

Andrés R. Alcántara[a], Pablo Dominguez de Maria[b], Jennifer Littlechild[c], Martin Schürmann[d], Roger Sheldon[e], Roland Wohlgemuth[f]

[a] Prof. Dr. Andrés R. Alcántara
Department of Chemistry in Pharmaceutical Sciences (QUICIFARM)
Complutense University of Madrid (UCM)
28040-Madrid, Spain
Email: andalcan@ucm.es

[b] Dr.habil. Pablo Domínguez de María
Sustainable Momentum, SL
Av. Ansite 3, 4-6
35011 Las Palmas de Gran Canaria
Canary Is, Spain

[c] Prof. Dr. Jennifer Littlechild
Henry Wellcome Building for Biocatalysis
Biosciences, University of Exeter, Stocker Road,
Exeter, EX4 4QD, UK
Email: J.A.Littlechild@exeter.ac.uk

[d] Dr. Martin Schürmann
InnoSyn B.V.
Urmonderbaan 22,
6167RD Geleen, The Netherlands
Email:martin.schuermann@innosyn.com

[e] Prof. Dr. Roger A. Sheldon
Molecular Sciences Institute, School of Chemistry
University of the Witwatersrand,
Braamfontein, Johannesburg, South Africa.

[f] Prof. Dr. Roland Wohlgemuth
Institute of Molecular and Industrial Biotechnology
Lodz University of Technology
90-537 Lodz, Poland
Email: roland.wohlgemuth.1@p.lodz.pl

Abstract: The role and power of biocatalysis in sustainable chemistry has been continuously brought forward step by step to its present outstanding position. The problem-solving capabilities of biocatalysis have been realized by numerous substantial achievements in biology, chemistry and engineering. Advances and breakthroughs in the life sciences and interdisciplinary cooperation with chemistry have clearly accelerated the implementation of biocatalytic synthesis in modern chemistry. Resource-efficient biocatalytic manufacturing processes have already provided numerous benefits to sustainable chemistry as well as customer-centric value creation in various industrial sectors, such as the pharmaceutical, food, flavor and fragrance, vitamin, agro, polymer, specialty and fine chemical industries. Biocatalysis can make significant contributions not only to manufacturing processes but also to the design of completely new value creation chains. Biocatalysis can now be considered as the key enabling technology of first choice to implement Sustainable Chemistry.

Introduction

The use of nature's catalysts, the enzymes, for carrying out sustainable processes is becoming increasingly important and is well placed to play a pivotal role in achieving the Sustainable Development Goals of the European Union and worldwide. The European Commission, through the European Green Deal [1] will position the EU economy towards a more sustainable future and will foster the United Nation's 2030 Agenda [2]. The use of biocatalysis is an essential part of this implementation of 'green chemistry' to achieve the goal of environmentally friendly industrial processes with maximum resource utilization and minimum waste generation in a circular bio-based economy [3].

Advances in the DNA sequencing of microbial (meta)genomes and enzyme engineering through directed evolution have enabled the rapid identification of new robust enzyme activities and optimization for industrial applications [4]. Enzymes, besides being already part of our everyday lives, are also used for the biocatalytic production of new and safer drug molecules for healthcare, new enzymes for the detergent, cosmetic and food industries. Enzymes are also finding use in the recycling of waste materials, such as plastics, and in carbon dioxide capture.

The use of improved bioinformatic approaches and the application of artificial intelligence methods to predict the three-dimensional structures of enzymes using software such as AlphaFold 2 [5] are providing a greater understanding of enzyme properties allowing them to be modified in a rational informed way.

The directed evolution approach as pioneered by Frances Arnold [6] relies on evolving and screening enzymes for those with the desired activities and properties [7] enabling the adaptation of enzymes to processes, process conditions or reactions new to nature. Advances in molecular biology and rapid screening, including miniaturization and microfluidic technologies for enzyme function assays, have led to wide-spread applications [8-10].

Once robust biocatalysts are identified or genetically designed, process development offers many options to adapt to real industrial conditions. Thus, enzymes can be used as whole cell biocatalysts or as isolated enzymes that are often immobilized to enable multiple recycling [11]. Moreover, synthetic biology approaches can be carried out either *in vivo* or *in vitro* using purified enzymes to construct new artificial enzyme cascades for new products or drug synthesis. Biocatalysts can accept a broad array of possible reaction media ranging from purely aqueous solutions – the traditional first choice for enzymes –, to water-free systems, solvent-free processes, or neoteric solvents. The latter options provide solutions to enhance substrate loadings with lower waste formation, and may be integrated with previous or posterior industrial chemical steps, if needed.

This paper highlights selected, already demonstrated important applications of biocatalysts and provides an insight into the future challenges that can be addressed by applied biocatalysis.

The role of biocatalysis in sustainable chemistry has been very clearly and dynamically developing step by step over many years [12-18], due to numerous advances and breakthroughs in molecular and engineering aspects of biocatalysis, leading to its current powerful toolboxes and methodologies for designing sustainable processes. With the growing attention to sustainability, the application of biocatalysis has been increasing in both research and industrial areas as its power is more widely appreciated [19]. It has been even recently stated that we are in a Golden Age of Biocatalysis [20].

Over the last two decades biocatalysis has played an increasingly important role as the method of choice in industrial organic synthesis of molecules of increasing complexity. For instance, relevant examples from ethical, top-selling pharmaceuticals are the biocatalytic processes for the cholesterol lowering statin drugs, like the aldolase enabled process to atorvastatin (Lipitor, Pfizer) and rosuvastatin (Crestor, AstraZeneca) intermediates developed and implemented by DSM/InnoSyn researchers [21-22] and the three enzyme process for the Pfizer cholesterol lowering agent, atorvastatin (Lipitor), developed by Codexis [23]. The nine-enzyme three-step cascade for the synthesis of the nucleoside HIV inhibitor, islatravir [24], or the short and sustainable synthesis of molnupiravir, a nucleoside-based anti-viral agent against SARS-CoV-2, developed in a collaboration between Merck and Codexis [25], further attest to the increasing importance of biocatalysis for manufacturing pharmaceuticals and their intermediates. The latter process, which will be discussed later, was enabled by the invention of an elegant biocatalytic cascade, employing engineered enzymes, from simple raw materials and involving only a single isolated intermediate. The enzymes were discovered, evolved and the resulting process implemented on a large scale within 6 months.

Biocatalytic processes are also playing an increasingly important role in the industrial production of natural food ingredients of increasing complexity through the directed in vitro evolution of biosynthetic enzymes that produce natural products in vivo [26]. For example, processes for the synthesis of the natural stevia

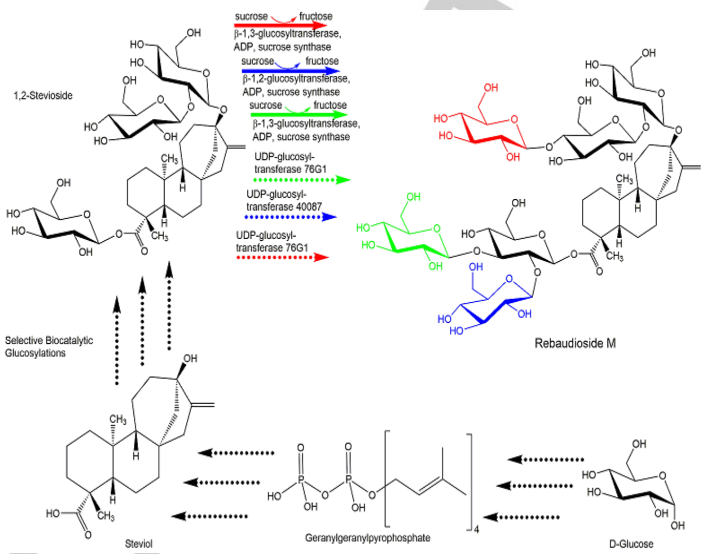

Figure 1. Biocatalytic *in vitro* synthesis (reactions indicated by plain arrows) as well as biocatalytic *in vivo* synthesis (reactions indicted by dotted arrows) of the natural stevia glycoside sweetener rebaudioside M

The Codexis/Tate & Lyle collaboration and the Matsutani/Kagawa University joint project have also developed a process (see figure 2) for the production of the sweetener, D-allulose by enzymatic epimerization of D-fructose [29-30].

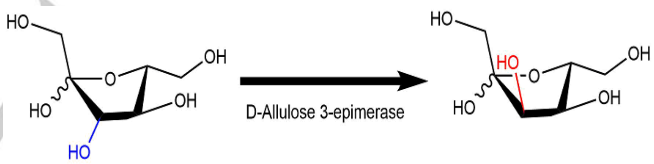

Figure 2. Biocatalytic process for manufacturing the sweetener D-allulose by epimerization of D-fructose

There are no broad-scope methods for ester and amide syntheses in water, because the aqueous media triggers the hydrolysis. Notably, this situation is rapidly changing through biocatalysis [31]. Acyl transferases catalyze the formation of esters and amides in water by performing the reactions under kinetically controlled conditions. For example, the acyl transferase from *Mycobacterium smegmatis* (MsAcT) exhibits high synthetic activity in water [32-34], including the formation of flavor esters [35], the acylation of primary amines [36], or peracid-mediated oxidations [37] in aqueous media. More recently, protein engineering has been used to obtain MsAcT variants exhibiting higher acyl transfer to hydrolysis ratios [38] and higher enantioselectivities [39] in catalytic transesterifications in water. Bornscheuer and coworkers [40] described a method for identifying new acyl transferases by analysis of amino acid sequence data. Furthermore, the scope of acyl transferase catalyzed esterifications was expanded to include the synthesis of sugar esters in water [41] and immobilized MsAcT was used for esterifications and amidations in continuous flow aqueous operations [42-43]. These synthetic approaches in water give clear hints on how biocatalysis can tackle reactions with high synthetic relevance.

Both whole-cell and cell-free biocatalysis are essential components of the envisaged defossilization of chemicals manufacture in the drive to a circular, carbon-neutral economy [44]. Biocatalysis will flourish in future biorefineries where carbohydrates, not hydrocarbons, will be the base chemicals. It will be used in the initial conversion of, for example, polysaccharide feedstocks to fermentable sugars and in down-stream processing of carbohydrate intermediates.

Biocatalysis can also play an important role in the production of commodity polymers which are the major, large-volume applications of bulk chemicals. In addition, they can play an important role in mitigating the pollution and degradation of our natural environment caused by the indiscriminate disposal of polymers. As a remarkable case, the future of plastics lies in their ability to be redesigned for recyclability [45]. Polyesters, for example can be produced from biomass and can then be recycled hydrolytically back to the original monomers to make new plastic. Polylactate and polyhydroxyalkanoates are examples of such bio-based plastics. It has also been demonstrated that polyethylene terephthalate can be hydrolyzed back to the monomers using an enzyme, PETase, that was isolated from a microorganism living in the soil of a PET recycling facility [46]. There is scope for the development of new thermophilic PETase enzymes which can be used for the industrial scale degradation of plastics at elevated temperatures close to the point where plastic transitions to a liquid rather than being a solid. This will improve the enzymatic degradation process and avoid any additional pre-treatment. Therefore, the engineering of thermostable PETase variants is important for effective PET hydrolysis [47].

Biocatalysis for Anti-virals against SARS-CoV-2

In the synthesis of anti-virals biocatalysis has already proven its value and has been important in the manufacture of anti-viral drugs and corresponding intermediates, long before the current COVID-19 pandemic. Biocatalytic methods are widespread and over 60% of all FDA-approved anti-viral agents or their inter-mediates have been made accessible through biocatalysis [48]. The benefits of advances in methodologies and platform technologies in biocatalysis are clearly evident as key for improving sustainability of chemical processes at industrial large scale. Significant advances have now moved biocatalysis forward towards the rapid and urgent process design phase in early drug discovery and development of a much-needed target compound. Molecular and engineering aspects of a process, such as the selectivity, adaptability and versatility, space-time yield, product recovery and purification, are thereby already taken into consideration from the beginning of the process design. This provides strategic advantages for the rapid development of biocatalytic processes at manufacturing scale, in particular in the develop-ment of drugs against SARS-CoV-2. Although the fast development of highly efficient vaccines represents a breakthrough and prevents SARS-CoV-2 infections, effective pharmaceuticals for the treatment of patients with virus infections are also required. Therefore, the recent achievements and the fast development of an efficient and sustainable biocatalytic process for the anti-viral prodrug molnupiravir (see figure 3), which targets the SARS-CoV-2 RNA-dependent RNA polymerase, are exciting developments [25].

Molnupiravir has been approved as the first oral anti-viral against SARS-CoV-2 by the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK under its tradename Lagevrio in November 2021 and received an emergency use authorization by the US FDA on 30 November 2021. An efficient biocatalytic synthesis of a key intermediate, *N*-hydroxycytidine, from cytidine as starting material can contribute to further improvements in the integrated biocatalytic production of molnupiravir [49]. This showcases outstandingly how biocatalysis can nowadays be rapidly adapted to global challenges, combining mild reaction conditions and efficiency.

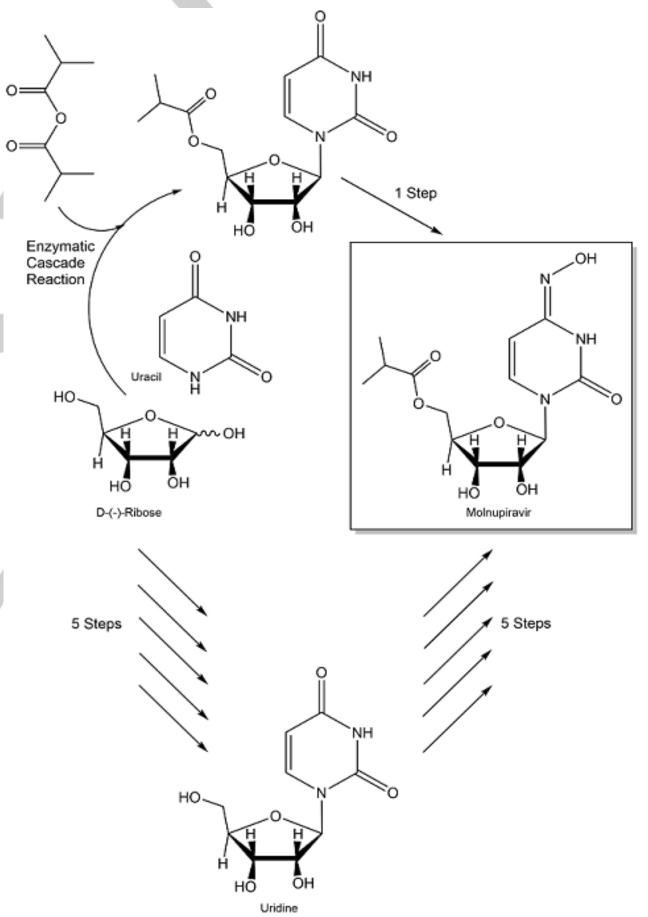

Figure 3. Efficient and sustainable biocatalytic process to the antiviral prodrug molnupiravir

The original 10 step chemical synthesis of molnupiravir with <10% overall yield has been shortened to a 3 step synthesis with 69% overall yield and only one isolated intermediate. This demonstrates the power and value of biocatalysis as a key enabling technology for the rapid industrial manufacture of this anti-viral agent (figure 3) using readily available raw materials and enzymes. It also shows the growing capabilities of biocatalysis in pharmaceutical early development for rapidly delivering novel sustainable routes at manufacturing scale.

System boundary conditions: biocatalysis at the forefront of sustainability

The key role of biocatalysis as a green chemistry and sustainability enabler has been clearly proven through many excellent examples [12, 17, 50-55]. It must be noted though, as pointed out recently [56], that the mere use of a biocatalyst in a chemical reaction does not assure its inherent sustainability. This has to be evidenced by means of the assessment of different chemometric parameters [57]. Several parameters have been proposed to reflect the environmental impact of a given synthetic reaction. Undoubtedly, the E-factor, defined as the kgs of "everything but the desired product" produced divided by kgs of product, including solvent losses and chemicals used in work-up [58], is the most frequently reported metric to quantify the actual amount of waste.

$$\textbf{E-factor (E)} = \frac{\text{mass of waste (kg)}}{\text{mass of desired product (kg)}}$$

Scheme 1. Definition of the E-factor

In fact, its simplicity, insightfulness, and broad applicability (E-factors of individual steps are additive and therefore easily calculated for single- and/or multi-step processes) make it extremely recommendable to evaluate any organic reaction. The ideal E-factor is zero which concurs with the first principle of Green Chemistry and stresses the ideal of preventing waste generation instead of implementing methods for its remediation [59]. Strictly speaking, the contribution of water and solvents must be considered in the calculation of E-factors, especially for aqueous biocatalysis, leading to cEF (complete E factors) [58], even if water and solvents are recycled, as they can be easily polluted in multi-step processes (see [56] for a practical example on the effect of water on E calculation).

Some modifications on the E-factor have been reported, derived from the fact that the E-factor neither reflects the different composition of waste materials (waste "quality"), nor categorizes them according to their possible environmental impact [57]. The introduction of an environmental quotient Q (accounting for the nature of the waste, and used as a multiplier of E) was reported [60]. For calculating Q, the use of the straightforward and easy-to-use EATOS (Environmental Assessment Tool for Organic Synthesis) software (available at http://www.metzger.chemie.uni-oldenburg.de/eatos/english.htm) is recommended [61]. It calculates the potential environmental impact (PEI) of waste by assigning different penalty points based on human and eco-toxicity (effects such as persistence, bioaccumulation, ecotoxicity). Similarly, a semi-quantitative post-synthesis tool, EcoScale, was reported by van Aken et al. [62], for estimating both economic and environmental impact factors of organic syntheses on a bench scale. The EcoScale assigns penalty points to six parameters (yield, cost, safety hazards, technical setup, reaction conditions, and ease of downstream processing), and subsequently subtracts the sum of all of them from 100. Thus, the closer to 100, the greener the synthesis. Another very intuitive approach, also based on deduction of penalty points from 100 is the Green Motion™ metric reported by Phan et al. [63]. In this methodology, using a questionnaire (yes/no answers), seven fundamental aspects (raw material, solvent used, hazard and toxicity of reagents, reaction efficiency, process efficiency, hazard and toxicity of final product and waste generation) are assessed by pictograms and numerical values, The penalty points, derived by the previous survey, lead to a score; the higher this score, the more sustainable and the smaller the environmental impact of the process.

On the other hand, and mainly for the production of bulk chemicals, the energy consumption is an important component to be considered, Therefore, the E$^+$ has been recently reported [64]. This metric factor considers the greenhouse gas emissions (as CO_2 emissions) generated from electricity used for processes such as cooling, heating, stirring and pumping.

$$\mathbf{E^+} = \text{E} + \frac{\text{W x CI}}{\text{mass of desired product (kg)}} \quad \begin{bmatrix} \text{W = electrical power used (kWh)} \\ \text{CI = carbon intensity } \dfrac{\text{kg } (CO_2)}{\text{kWh}} \end{bmatrix}$$

Scheme 2. Definition of the E$^+$-factor

Aiming at broadening the analysis of the environmental impact, Christensen et al. [65] proposed the use of the Climate Factor (C-Factor) in order to quantify the carbon footprint of chemicals. This C-factor is defined as the total mass of CO_2 emitted divided by the mass of product formed (kg CO_2 / kg product).

$$\textbf{(C)limate Factor} = \frac{\text{total mass of } CO_2 \text{ emitted}}{\text{mass of product formed}} \quad \textbf{(kg } \mathbf{CO_2}\textbf{/ kg product)}$$

Scheme 3. Definition of the C-Factor

This metric, accounting for the overall kg of CO_2 emitted both in the production of the raw material(s) and also in its (their) conversion into the final product(s), is especially suitable for comparing biomass *vs* fossil resource-based processes [66].

Process Mass Intensity (PMI) [67] is the total mass of all chemicals used in a process divided by the mass of desired product and is equal to E + 1. The ideal PMI is 1. It must be noted, however, that calculating the gate-to-gate mass efficiency metrics of a (bio)catalytic reaction represents only the first step in the quest for green and sustainable processes. These parameters must be complemented with more holistic and broader studies, such as Life Cycle Assessments (LCA). These studies cover not only the reaction as such, but also the "pre-chains" impact - origin of the substrates, catalyst production, and transportation - as well as the "post-chains" impact of product delivery and final disposal, ideally in circularity means.

Identification of future challenges in biocatalysis

Although biocatalysis has become a key scientific and technological area which enables the use of more sustainable raw materials, new processes, intermediates and products, the many dimensions involved need to be considered regarding the existing and future boundary conditions. It is therefore of paramount importance to identify new future challenges which are relevant to the levels of fundamental molecular and engineering sciences, new product research and development and manufacturing, from laboratory to industrial scale.

From a systems level perspective, a number of future challenges can be envisioned. These can be assembled into missions:

- developing the biocatalysis-information and communication technologies (ICT) interface to enable rapid and meaningful access to enzyme structure-function information, kinetic and thermodynamic characteristics of enzymatic reactions as well as the communication and storage of meaningful and relevant data

- discovering and engineering novel classes of enzyme functions, for catalyzing natural and/or new to nature reactions

- discovering and engineering novel properties of known enzymes and rapid development tools and methodologies to obtain the optimal catalytic performance

- developing (cost-)efficient biocatalytic systems for the (controlled/defined) degradation of the industrially most relevant polymer types (such as polyesters, polyamides, polyurethanes etc.) to enable their recycling in the same quality and for the same polymer application

- developing (redox) co-factor or co-substrate supply and regeneration for bulk chemicals production that exceed the ones established for fine and pharma chemicals in atom and cost efficiency

- developing broad, reliable and scalable biocatalytic reaction platforms, including non-conventional reaction media beyond aqueous systems

- developing faster and more generic molecular and engineering methods to stabilise enzyme classes to the level of lipases and proteases for the challenging conditions in low-cost applications

- integrating biocatalysis into synthesis route planning and total synthesis in organic chemistry (retrosynthetic biocatalysis) [68-70]

- interfacing the molecular and engineering aspects, product recovery and purification and raw material utilization towards overall sustainable processes in industrial chemistry

- developing biocatalysis in flow for more efficient, more cost-effective processing

- developing scalable electro- and photo-biocatalysis [44]

- further developing IT tools and parallelized reactor set-ups for prospective LCA analyses to enable early stage fact based route selections [71] instead of estimations and experiences

In order to make full use of the power of biocatalysis in sustainable chemistry, factors hindering its application and specific bottlenecks need to be identified and analyzed. Interdisciplinary communication and problem-solving skills need to be implemented at different levels.

Emerging biocatalysis research areas, methodologies and tools

A large variety of novel biocatalysis tools and methodologies which have been developed in the past decades have increased the perception and status of biocatalysis, both in academia and industry [12-20, 72]. This very positive trend, which is accompanied by a number of newly emerging biocatalysis areas, can therefore be expected to continue and even accelerate, if supported accordingly, over the next 10 years.

Several orthogonal and mutually beneficial developments have come from bottom-up approaches. Versatile biocatalytic reaction platforms provide the experimentally rooted background for extending the scope of classical and new reaction classes, such as selective biocatalytic hydrolyses [73], oxidations [74], reductions [75], glycosylations [76], phosphorylations [77], methylations and fluoromethylations [78-79], addition [80] and elimination reactions [81], and carboxylations [82-83].

The development of new-to nature biocatalytic reactions [84] enables biocatalysis to enter completely new fields, such as sustainable silicon chemistry [85].

Biocatalytic reaction platforms, metabolic engineering and synthetic biology can be valuable in a systems biocatalysis approach [86] to biocatalytic route design from raw materials or waste materials, *e.g.* carbon dioxide [87], to useful products. Emphasis on combining the use of biocatalysis and biobased starting materials is also useful for a sustainable virtuous cycle in a biorefinery-like approach.

Sustainable value creation in industrial sectors for the application of biocatalysis

Customer-centric value creation by the application of resource-efficient biocatalytic manufacturing processes has already been providing numerous benefits to sustainable chemistry in various industrial sectors, such as the pharmaceutical and life science industries, flavor, fragrance, cosmetics and personal care industries, vitamin, food and drink industries, agrochemical industry, polymer, specialty and fine chemical industries [88-92]. For example, from a number of chemical and pharmaceutical companies in Switzerland there are indications that biocatalysis implementation is on the move in chemical manufacture, as every year an increasing number of companies consider the use of enzymes in chemical synthesis [93].

The privilege of the inherent chirality and evolvability of biocatalysts is especially valuable for developing advantageous reaction platforms with improved selectivity and sustainability for industrial sectors in which catalytic asymmetric synthesis is essential for manufacturing. Examples of the growing number of biocatalytic reaction platforms applied in asymmetric synthesis at industrial scale include ammonia addition, oxidation and cyclization, which are illustrated below.

Early analyses of ecological benefits of replacing conventional chemical process with biocatalytically enabled chemo-enzymatic processes came from the pharma sector. Researchers from

DSM/InnoSyn developed and implemented a 2 or 3-step process, de-pending on the choice of starting material, for the ton-scale production of the non-natural cyclic amino acid (*S*)-2,3-dihydro-1*H*-indole-2-carboxylic acid [94]. This way a 7-step process involving classical resolution with 50% maximum yield could be replaced (see figure 4). In the new chemo-enzymatic process the phenylalanine ammonia lyase (PAL) catalyzed enantioselective ammonia addition to a cinnamic acid derivative could be tele-scoped into the cyclisation to the final product in water. This copper ion catalyzed cyclization was even possible with the low concentration of copper ions in the process tap water [94]. An LCA comparison of the two processes conducted according to the IPCC GWP 100a procedure at the production site revealed that the CO_2 footprint of the new chemo-enzymatic process was reduced more than 2-fold from 280 to 125 kg CO_2 equivalents per kg of product compared to the old process [95].

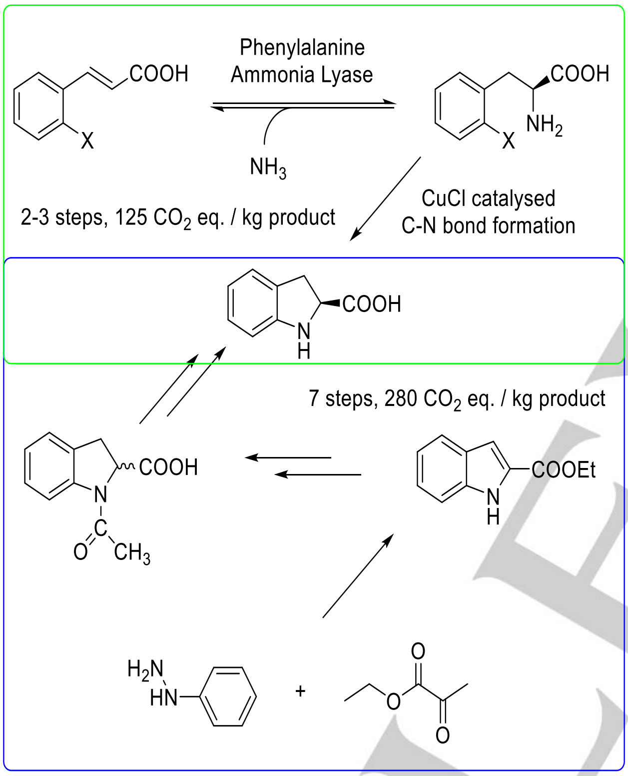

Figure 4. Chemo-enzymatic process to a chiral cyclic amino acid for pharmaceutical product intermediate. The biocatalysis enabled reduction of process steps leading to a significant reduction of CO_2 footprint.

Selectivity, controllability, scalability, safety, health and environ-ment issues of asymmetric oxidations are particularly important at industrial scale and large-scale processes using biocatalysts in non-flammable aqueous media and air as the terminal oxidant have been of much interest. From the many biocatalytic asymmetric oxidations which are catalyzed by Baeyer-Villiger monooxygenases, the example of the biocatalytic asymmetric sulfoxidation of pyrmetazole to the (*S*)-enantiomer of omeprazole (see figure 5) demonstrates not only superior chemo- and enantioselectivity but also provides productivity, cost and environmental benefits [96].

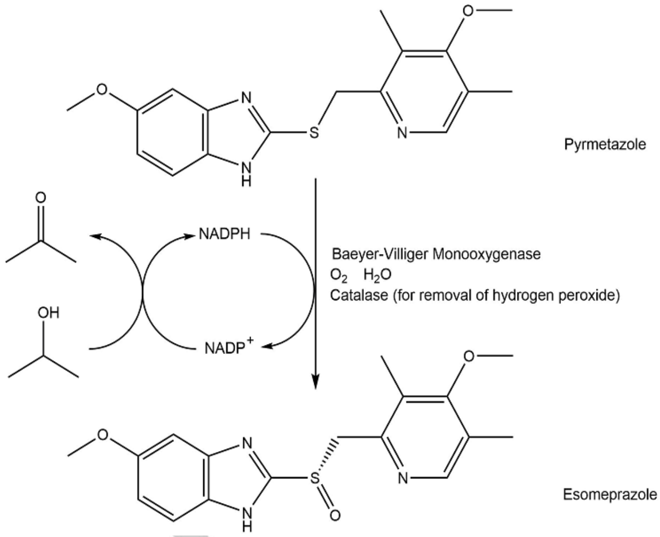

Figure 5. Biocatalytic asymmetric sulfoxidation of pyrmetazole to the (*S*)-enantiomer of omeprazole utilizing Baeyer-Villiger monooxygenase, catalase and ketoreductase/isopropanol for cofactor regeneration provides an efficient process with high catalytic efficiency and compares favorably with the Kagan−Sharpless−Pitchen sulfoxidation

The development of a scalable biocatalytic cyclization process of (*E,E*)-homofarnesol to (−)-Ambrox catalyzed by squalene hopene cyclase (see figure 6) demonstrates not only the value of enzyme and reaction engineering towards process-relevant conditions but also the sustainability benefits of the biocatalytic production process of the fragrance ingredient (−)-Ambrox [97].

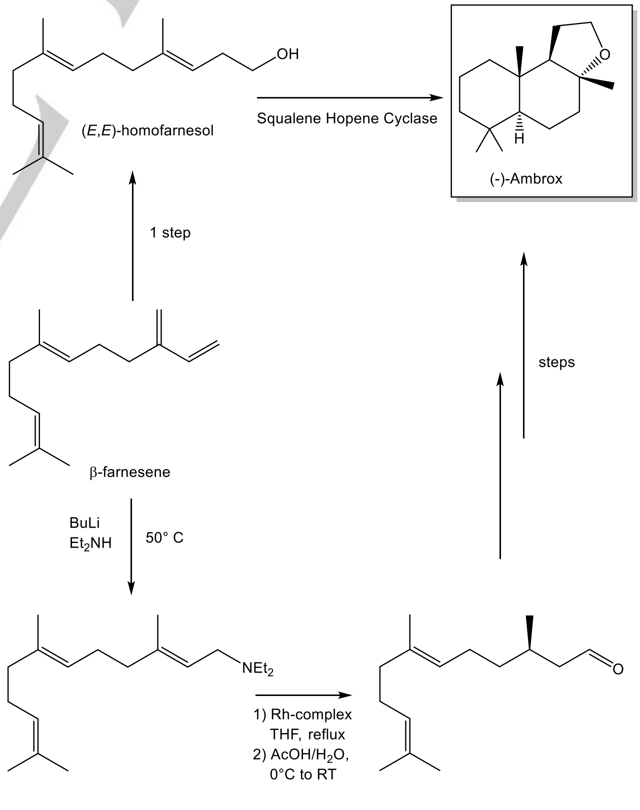

Figure 6. Biocatalytic synthesis of (-)-Ambrox not only improves atom and step economy, but also reduces waste, solvent, energy and noble metals compared to a chemocatalytic route.

Rolling out biocatalysis globally at all levels

As reflected in the introduction, the European Commission, through the European Green Deal [1] is strongly committed to renovate the European Union's (EU) economy for a more sustainable future and to foster the implementation of the United Nation's 2030 Agenda and the Sustainable Development Goals (SDGs) [2]. In fact, the Green Deal is mandating the EU to become a sustainable climate neutral and circular economy by 2050, also setting the objective to better protect human health and the environment, by tackling pollution from all sources and moving towards a toxic-free ecosystem.

Chemicals are ubiquitous in our daily lives, playing a pivotal role in most of our activities, as they are the building blocks of low-carbon, zero pollution and energy- and resource-efficient technologies, materials and products. Therefore, the European Commission has developed a chemical strategy for implementing sustainability in our common path to a toxic-free environment [3]. In this scenario, and aligned with the first principle of Green Chemistry (preventing waste generation instead of implementing methods for its treatment and/or removal [98]), the European Commission has recently launched the Sustainable-by-Design (SbD) criteria, with the purpose of providing a framework allowing the definition of a set of criteria to increase the safety and sustainability of chemicals, materials and products [99]. In the overall context, catalysis is undoubtedly a very powerful tool to fulfil all the above-mentioned sustainability criteria [100]. In particular, the green and sustainable credentials of biocatalysis are beyond any doubt [12, 17, 19, 51-55]. The exquisite precision of biocatalysts (in terms of chemo-, regio- and stereoselectivity), combined with their biodegradability, non-toxicity and capability for catalyzing a broad palette of reactions under very mild reaction conditions, makes them extremely powerful [101]. Nowadays, the combination of these advantages with the rapid implementation of enzymatic processes (when needed, as in the SARS-CoV-2 example) at industrial level, gives an exciting view of the future for biocatalysis as a core technology to reach sustainability and efficiency in chemical processes. Biocatalysis is a key enabling technology for a resource-efficient chemical industry and for novel value creation architectures in the global bio-economy [102-103], and is perfectly equipped to address the future challenges towards a sustainable future.

Conclusion

Biocatalysis has over the past decades evolved from being a niche and specialty area of catalysis, to be only considered when all other synthetic chemistry methodologies fail to deliver the desired products, to a key enabling technology providing powerful synthetic tools and methodologies to complement chemistry. Biocatalysis is nowadays in an excellent position to successfully tackle the challenges of the science of synthesis from the beginning of the process design. It additionally addresses the safety, health, economic and environmental boundary conditions, when applied to large scale industrial production. The tremendous advances and breakthroughs of the life sciences have clearly accelerated the implementation of biocatalytic synthesis in chemistry as evidenced by its rapid implementation in the synthesis of much needed anti-viral agents. The advantages of biocatalysis have also been outlined for various other industrial sectors beyond the pharmaceutical industry, where biocatalysis can make significant contributions to sustainable chemistry.

Importantly, drawing a sustainable track for the current decade it is important to consider biocatalysis as a technology of first choice and as a key pillar for a Green Deal.

The track to global sustainability will clearly benefit from firm long-term commitments by all stakeholders for missions which address future challenges ranging from fundamental molecular and engineering sciences to applications in new product research, development and manufacturing, from laboratory to industrial scale. The further advancement and implementation of biocatalytic technologies requires continued investments, including investment also in education and training of skilled scientists. It is imperative that the further development and use of these clean and green technologies is jointly brought forward by science, industry and society, thus contributing to the development of the Sustainable Chemistry of the future.

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Keywords: Biocatalysis • Industrial Chemistry • Advanced Manufacturing • Sustainable Chemistry • Green Deal

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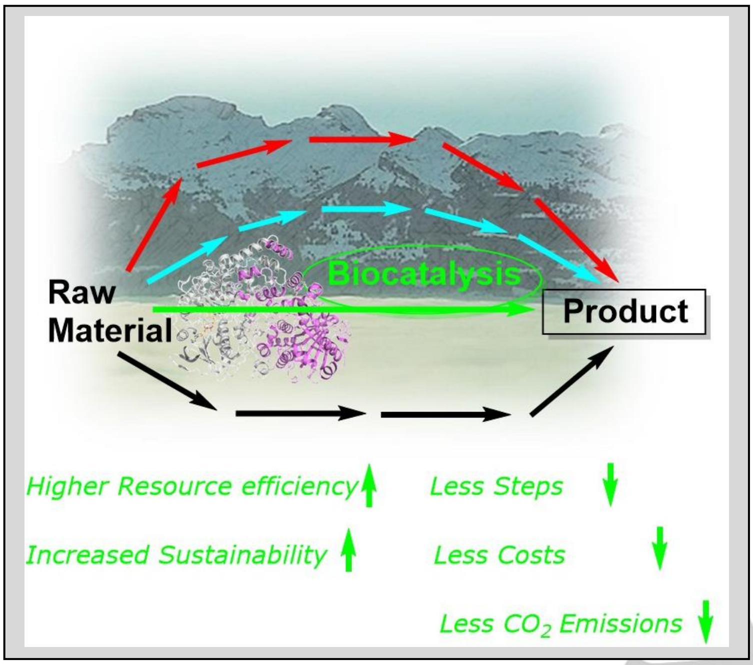

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