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Biocatalysis for Organic Synthesis

Amol Bhosale

Abstract: ***The applications of biocatalysis for synthesis of organic molecules has attracted to chemist over past few years.Enzymes as a biological catalyst play an important role in the synthesis of key intermediates for the pharmaceutical and chemical industry. Enzymes are also plays vital role for synthesis of selective molecules. Biocatalyst is also called a green catalysts because bio catalyticsynthesis is theenvironment friendly. Biocatalysts like oxidoreductases, transferases, hydrolases, lyases, isomerases will be discussed in this reviewwith their advantage and major enzyme catalysts in industrially use.***

Keywords: Biocatalysis, Selectivity, Acyl transferases, Hydrolytic Enzymes

1. Introduction

Bio catalyst is increasingly being used to assist in synthetic routes to complex molecules of industrial interest. There is a particular interest in the use of biocatalyst to create new routes to lower value chemicals. Biocatalyst (usually enzymes, whole cells, or microorganisms) is used to speed up chemical conversions. Enzymes are derived from plants, animal tissue, micro-organisms like yeast, bacteria or fungietc. They are complex protein molecules formed within living cells and can function in vitro. Biocatalysts have all the properties of a chemical catalyst and they carry out reactions in free or immobilized form. The advantages of enzymes include their ability to carry out specific chemical transformations, which are easy to control and can be operated in the mild range of reaction conditions like temperatures (~20-40 C) and pH (typically 5-8) and are completely biodegradable[01]-[05].Enzymes catalysts can be used for the synthesis of organic solvents, as they carry out highly selectivetransformations. The properties of enzymes like selectivity, stability, activity, and substrate specificity are routinely engineered for specific end-uses. They can be used to convert chiral molecules three-dimensionalpurespecific asymmetric processes as it can easily distinguish between shape and functionality, either within given molecule or in a mixture of molecules due to their unique three dimensional shapes[6].Enzymes have such effective propertiesit can replace the conventional chemicals simultaneously for saving energy and water in the production processes[07]-[08].

Enzymatic conversions minimize the problems of undesired side- reactions like isomerization, decomposition, rearrangement & racemization. Thus, biocatalysts has proved its superiority over traditional chemical synthesis pathways in many ways. Biocatalysts process is an important tool and widely used for the products ranging from knowledge chemicals to the commodity chemicals. Several novel applications of biocatalysts are evolving rapidly nowadays. High selectivity of enzymes results in cost optimization, a major reason for using the process[09]-[10]. For industrial purposes, cost of biocatalyst can be reduced by reusing stabilized enzyme preparations by immobilization technique[11]. The microorganisms used for the enzyme production are grown using the optimized media in a fermenter. The produced enzymes may be extracellular (i.e. secreted in the medium) or intracellular[12]-[13].

2. Classification of Enzymes

2.1 Oxidoreductases

They catalyze oxidation and reduction reactions that occur within the cell involving oxygenation or overall removal or addition of hydrogen atom equivalents. These types of enzymes are widely used in industrial reactions. Examples of such class of enzymes include dehydrogenases, oxidases, oxygenases, peroxidases.

2.2Transferases

They catalyze the transfer of functional groups (e.g. amino, methyl groups) by means of a nucleophilic substitution reaction. The industrial applications of transferases include the use of various glycosyltransferases for the synthesis of oligosaccharides. Examples of transferases enzymes include methyltransferases, aminotransferases, kinases, phosphorylases.

2.3 Hydrolases

They catalyze the addition of water to a substrate (hydrolysis). Hydrolytic enzymes are more commonly used in organic synthesis to produce intermediates for pharmaceuticals and pesticides. Examples of this class include phosphatases, amidases, proteases, esterases, and lipases.

2.4 Lyases

These enzymes are responsible for catalyzing addition and elimination reactions. Lyases are enzymes cleaving C-C, C-O, C-N, C-S, and other bonds by elimination, leaving double bonds or rings, or conversely adding groups to double bonds. The type of Lyases enzymes are found in cellular processes in organic synthesis, citric acid cycle, and in the production of cyanohydrins. Examples of this class of enzymes include decarboxylases, aldolases, synthases.

2.5 Ligases

They catalyze the formation of bonds between two molecules or they join two molecules. Ligases catalyze ,reactions that involve the creation of chemical bonds with nucleotide triphosphates. Examples of this class of enzymes include synthetases, carboxylases.

2.6 Isomerase

These types of enzymes catalyze the rearrangement of atoms within molecules such as racemization and epimerization. The enzymes exhibit a unique specificity relative to the reactions they catalyze[14]-[16].

3. Advantages of Biocatalysis

Biocatalysts increase the speed of chemical reactions similar to chemical catalysts, without any thermodynamic change. They offer some unique characteristics over conventional catalysts [17]-[18].

The keyword organic synthesis is selectivity which is necessary to obtain a high yield of a specific product. There is a large range of selective organic reactions available for most synthetic needs. There is still one area where organic chemists are struggling for achieving chirality, but now a days considerable progress is being in chiral synthesis has been achieved in past years. Enzymes display three major types of selectivity.

Chemo selectivity: Since the purpose of an enzyme is to act on a single type of functional group, other sensitive functionalities, which would normally react to a certain extent under chemical catalysis, survive. As a result, bio catalyticreaction is to be "cleaner" and laborious purification of the product(s) from impurities emerging through side-reactions can largely be omitted.,

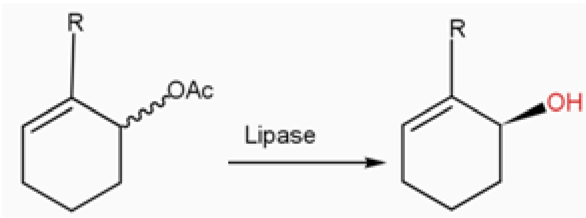
Regio selectivity: Enzymes have their three-dimensional structure, they may distinguish between functional groups,which are chemically situated in different regions of the substrate molecule.

Enantioselectivity: Enzymes are made from L-amino acidsand because of these enzymes are chiral catalysts. Chirality present in the substrate molecule and is recognized upon the formation of the enzyme-substrate complex. Thus a pro-chiral substrate may be a transformation into an optically active product and both enantiomers of a racemic substrate may react at different rates.The interest in turn in to biocatalyst is mainly due to the need to synthesize enantiopure compounds as chiral building blocks for drugs and Agrochemicals. Another important advantage of biocatalysts is that they are environmentally acceptable, being completely degraded in the environment. Enzymes act under mild conditionswhich minimizethe problems of undesiredside-reactions. One another aspect of the biocatalysts isthey are stable in moderate condition and reaction can be done in an aqueous environment[19]-[21].

4. Acyl Transferases

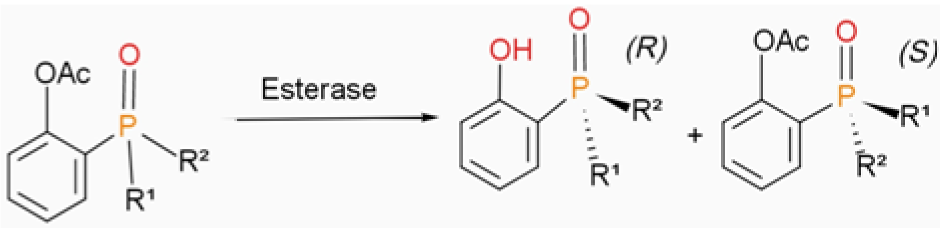
4.1 Lipase

Among the biocatalyst in organic synthesis, lipase is the most frequently used. In particular, this class of enzyme is able to perform enantioselective hydrolytic reactions and because ofthis role, they are most frequently employed. lipases have been extensively utilized in the synthesis of many biologically active compounds and natural products[22].



4.2 Esterase

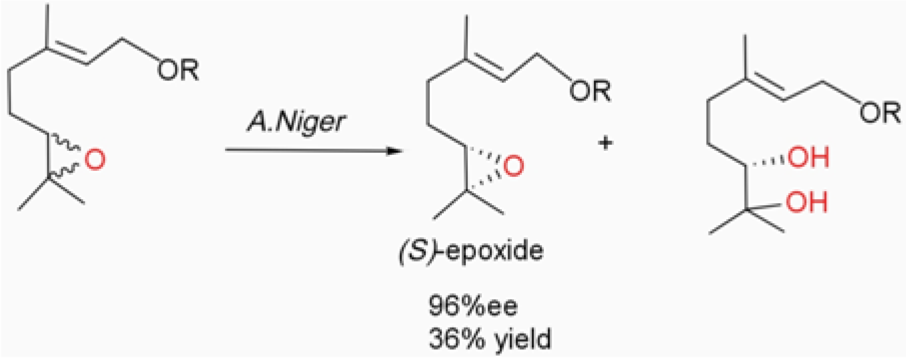
Esterases are a diverse group of hydrolases enzyme. Esterase catalyze the cleavage bond reaction and formation of ester bonds. Esterasealso shows high regio- and stereospecificity, which makes them attractive biocatalysts for the synthesis of optically pure compounds[23]-[24].



5. Hydrolytic Enzymes

5.1 Epoxidases

Epoxidases are enzymes that catalyze the hydrolysis of an epoxide to furnish the corresponding vicinal diol.The configuration of the resultant diol can be retained or inverted, depending upon the regioselectivity of the enzymes and the substituent's on the carbon atom involved. For example, epoxidasehas been used for the hydrolysis of different mono-di-tri-substituted and styrene-oxide type epoxides.More recently the epoxidase from A.niger was used for the preparative hydrolysis of glycidylacetal derivatives, which are difficult to obtain by purely chemical methods[16].



5.2 Nitrilases and Nitrile Hydratases

These enzymes are responsible for the biodegradation of nitriles. Nitrilasescatalyze the direct hydrolysis of nitriles to the corresponding acids whereas nitrile hydratases catalyze the hydration of nitriles to the corresponding amides. The high functional group flexibility of nitriles as intermediates in synthesis has driven much of his work as exemplified by the use of these enzyme catalyzed hydrolyses for the preparation of various enantiomerically enriched targets [25].

6. Conclusion

In conclusion, enzyme catalysis have become an attractive synthetic tool for synthesis of organic molecules. Today a different organic reactions like redox reactions, hydrolytic reactions, transfer reactions, carbon–carbon bond formation etc. can be carried out by efficiently usingbiocatalysts. The key word for organic synthesis is selectivity or chirality,which is necessary to obtain a high yield of a specific product. There is a large range of selective organic reactions available for most synthetic needswhich would be achieve with enzyme catalyst.

References

[1] Ager DJ, Li T, Pantaleone DP, Senpeil RF, Taylor PP, Fotheringham IG. Novel Biosynthetic routes to non-proteinogenic amino acids as chiral pharmaceutical intermediates. J. Mol. Catal. B:Enzymatic 11,2001,199-205.

[2] Reetz, M.T. Biocatalysis in organic chemistry and biotechnology: Past, present, and future. J. Am. Chem. Soc.2013, 135, 12480–12496.

[3] Anastas, P.T. Introduction: Green chemistry. Chem. Rev. 2007, 107, 2167–2168.

[4] Chapman, J.; Ismail, A.E.; Dinu, C.Z. Industrial Applications of Enzymes: Recent Advances, Techniques and Outlooks. Catalysts 2018, 8, 238.

[5] Turner, N.J.; Kumar, R. Editorial overview: Biocatalysis and biotransformation: The golden age of biocatalysis.Curr. Opin. Chem. Biol. 2018, 43, A1–A3.

[6] Milner, S.E.; Maguire, A.R. Recent trends in whole cell and isolated enzymes in enantioselective synthesis,Arkivoc 2012, 321–382

[7] Sheldon, R.A. The E factor 25 years on: The rise of green chemistry and sustainability. Green Chem.2017, 19, 18–43.

[8] Tickner, J.A.; Becker, M. Mainstreaming green chemistry: The need for metrics. Curr. Opin. Green Sustain.Chem. 2016,1, 1–4.

[9] Roberts S.M, Kozhevnikov I. Derouane E. Catalysts for Fine Chemical Synthesis: Hydrolysis, Oxidation and Reduction. Volume 1. Edited by Stan M Roberts and Geraldine Poignant Copyright (c) 2002 John Wiley & Sons, Ltd.(2002).ISBN: 0-471-98123-0, 5-11

[10] Roger Sheldon,.Introduction to Green Chemistry, Organic Synthesis and Pharmaceuticals. Green Chemistry in the Pharmaceutical Industry. Edited by Peter J. Dunn, Andrew S. Wells and Michael T. Williams2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.2010. ISBN: 978-3-527-32418-7, 1-20.

[11] Polizzi, K.M.; Bommarius, A.S.; Broering, J.M.; Chaparro-Riggers, J.F. Stability of biocatalysts. Curr. Opin.Chem. iol. 2007, 11, 220–225.

[12] Ward, T.R.; Köhler, V. Editorial overview: Biocatalysis and biotransformation: Bio-inspired, bio-based andbio-linked catalysis. Curr. Opin. Chem. Biol. 2015, 25, 5–6.

[13] Arturo Cano-Flores, Javier Gómez,Iker S. Escalona-Torres and Benjamín Velasco-Bejarano, Microorganisms as Biocatalysts and Enzyme Sources DOI:http://dx.doi.org/10.5772/intechopen.90338.

[14] Junhua A.T., Guo-Qiang L., Andreas L. (2009). Biocatalysis for the Pharmaceutical Industry. John Wiley & Sons Asia (Pte) Ltd. 1-19.

[15] Faber, K. (2011). Biotransformations in Organic Chemistry, DOI 10.1007/978-3-642-17393-6_2, Springer-Verlag Berlin Heidelberg. 32-313.

[16] Harald Groger and Yasuhisa Asano (2012), Principle of Enzyme catalysis, Third Edition. Edited by KarlheinzDrauz, Harald Groger, and Oliver May. © 2012 Wiley-VCH Verlag GmbH & Co. KGaA. Published 2012 by Wiley-VCH Verlag GmbH & Co. KGaA.

[17] Geoffrey A. B., Anke H., Santosh K. P., Sebastian S., and Uwe T. B. (2011). Discovery and Protein Engineering of Biocatalysts for Organic Synthesis. Adv.Synth.Catal. 353, 2191-2215.

[18] Bettina M. Nestl, Stephan C. Hammer, Bernd A. Nebel, and Bernhard Hauer (2014) New Generation of Biocatalysts for Organic Synthesis .Angew. Chem. Int. Ed. 53, 3070–3095.

[19] Kavita K., Kulkarni A.D.,Hussein S. H.(2011). Application of Biocatalyst in Chemical Engineering. International Journal of Advanced Engineering Technology, 2(4), 506-508

[20] Rubén de Regil and Georgina Sandoval. (2013). Biocatalysis for Biobased Chemicals. Biomolecules, 3, 812-847.
[21] T. Pohl, E. Niigele, H. Waldmann (1994) Biocatalysts as chemo- and regioselecting tools in organic synthesis. Catalysis Today, 22(3) 407-426.
[22] Paulina Majewska, Monika Serafin, Magdalena Klimek-Ochab, MałgorzataBrzezin´ ska-Rodak,EwaZyman´ czyk-Duda, 2016, Lipases and whole cell biotransformations of 2-hydroxy-2-(ethoxyphenyl phosphinyl) acetic acid and itsester, http://dx.doi.org/10.1016/j.bioorg.2016.02.011.
[23] M Morikawa, M Inoue, M Tsuboi, T Shomura, S Someya, S Murata, K Umemura, M Sugiura,JPharmacobiodyn. 1982 May; 5(5):314-8.
[24] Bertau, M.; Jeromin, G.E. Hydrolysis and transacylation: Esterases, lipases, phosphatases, and phosphoryl transferases. In Biocatalysis in Organic Synthesis,ed.; Faber, K., Fessner, W.D., Turner, N.J., Eds.; Georg ThiemeVerlag: Stuttgart, Germany, 2015; Volume 1, pp. 129–187.
[25] D.Brady, A.Beeton, J. Zeevaart, C. Kgaje, F. van Rantwijk, R. A.Sheldon, Characterisation of nitrilase and nitrile hydratase biocatalytic systems, Appl Microbiol Biotechnol (2004) 64: 76–85.