

Edited by Vicente Gotor, Ignacio Alfonso,  
and Eduardo García-Urdiales

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# Asymmetric Organic Synthesis with Enzymes



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*Edited by*

*Vicente Gotor, Ignacio Alfonso, and Eduardo García-Urdiales*



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*Eduardo García-Urdiales*

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## Preface

The increasing interest for obtaining chiral enantiopure organic molecules has tremendously expanded the development of new technologies and synthetic procedures pursuing this goal. Besides, a need for higher sensibility in developing environmentally friendly and sustainable processes is mandatory for the science and technology of the 21st century. Enzymatic processes combine both aspects with a high degree of success, being able to solve conceptual and practical problems. These are the main reasons for the increasing use of biotransformations both in academia and industry. The recent developments in molecular biology and biochemical tools have expanded the real applications of biotransformations, even on very large scales, and has broad applications in pharmaceutical, alimentary and cosmetic industries, just to cite a few. Enzymes work under very mild reaction conditions with a high degree of efficiency and selectivity. These facts constitute the foundations of an already well documented research field with very solid bases, but continuously expanding thanks to new techniques and methodologies. For this reason, we felt necessary to collect and organize these different bio-catalytic approaches to the synthesis of enantioenriched, ideally enantiopure organic compounds.

The book discusses most of the existing biocatalytic solutions to real synthetic problems, which makes it particularly helpful for synthetic, fine-chemicals and pharmaceutical chemists. In all chapters our goal has been to be comprehensive and clear enough in order to also make it a friendly-to-use source of information for undergraduate and PhD students aiming to enter into this fascinating and useful research area. Thus, we believe that this book can be both a tool for studying and a bench-guide for solutions to real problems.

The book has been divided in two main parts: one about methodology and a second one about synthetic applications. The first methodological part comprises three chapters focused on the different ways of improving the stereochemical outcome of a given biotransformation. The first chapter describes the different strategies available to improve the stereochemical outcome of a biocatalyst by modifying the reaction medium. The second chapter summarises the improvement of the enzymatic selectivity by generating new catalysts through directed evolution

techniques. Finally, a third chapter describing different methods available to find new enzymes with improved properties fulfills the methodology part of the book. The second and larger part has been organized attending to the type of reaction catalyzed by the enzyme or the conceptually special approach. Thus, the fourth chapter deals with dynamic kinetic resolutions, an elegant and attractive way of overcoming the 50% maximum theoretical yield of classical resolutions. Two other conceptually interesting and useful approaches, such as deracemization and enantioconvergent processes, are reviewed in chapter five. The sixth chapter presents the most recent uses of enzymes in the transesterification and hydrolysis of carboxylic acid derivatives, alcohols and epoxides, which are among the most widely used applications of enzymes in organic synthesis. In chapter seven, we have tried to compile the most recent advances in using enzymes for the resolution of amines and amide synthesis. Chapters eight and nine deal with reduction and oxidation reactions, respectively, specifically with the goal of obtaining enantioenriched interesting chiral compounds. Additionally, some intelligent solutions for the regeneration of the cofactors needed for the processes are specially highlighted. Finally, the formation of carbon-carbon bonds using enzymes is reviewed in the last chapter of the book.

We would also like to thank very warmly all the chapter authors who have felt the importance of producing a book with these characteristics. They clearly understood the philosophy of the project from the beginning, and they have contributed with exceptionally well-written pieces of work in all senses. We really would like to thank them for their highly enthusiastic dedication. We must say that it has been a real pleasure to collaborate with such an excellent group of scientist from all over the world.

And last but not least, we would also like to acknowledge the patience of our families and co-workers who, even without participating in this book, have suffered from the time and dedication devoted to this goal.

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## Methodology



