Edited by Wolf-Dieter Fessner
and Thorleif Anthonsen

WILEY-VCH

Modern Biocatalysis

Stereoselective and Environmentally Friendly Reactions

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WILEY-VCH Verlag GmbH & Co. KGaA

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Cover Illustration:
Background: Modified part of the "Biochemical Pathways Chart", 4th edition, by courtesy of F. Hoffmann-La Roche Ltd.

Protein structure taken from the RSCB Protein Data Base and modified:
PDB ID: 1ADO
N. Blom, J. Sygusch, Product binding and role of the C-terminal region in class I D-fructose 1,6-bisphosphate aldolase, *Nat. Struct. Biol.* **4** (1997), 36–39

Library of Congress Card No.:
applied for

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library.

Bibliographic information published by the Deutsche Nationalbibliothek
The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at http://dnb.d-nb.de.

Typesetting SNP Best-set Typesetter Ltd., Hong Kong
Printing Strauss GmbH, Mörlenbach
Binding Litges & Dopf GmbH, Heppenheim

Printed in the Federal Republic of Germany
Printed on acid-free paper

ISBN: 978-3-527-32071-4

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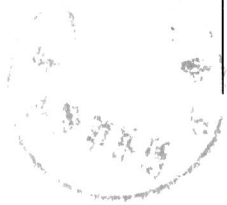

Preface

Asymmetric compounds cover a steadily increasing market share, e.g. as fine chemicals, chiral intermediates or pharmaceutical ingredients. The worldwide commercial volume of single isomers of chiral drugs currently approaches US$200 billion. Chirality dictates how stereoisomers interact with biological systems. Because of the often much improved biological specificity profiles of pure enantiomers as compared to their racemates, methods for resolving racemates and for preparing single enantiomers are in high demand. For the challenge of asymmetric synthesis to generate complex chiral compounds in high enantiomeric purity and yield, biocatalysis offers a tremendous advantage due to the homochiral nature of protein catalysts, which offer unparalleled levels of stereoselectivity and reaction specificity, in addition to their remarkable catalytic efficiency under mild conditions and regenerative production from biological materials. Breakthrough technologies in modern molecular biotechnology research, development and application have recently paved the way for the rapid discovery and engineering of novel enzymes, and today allow the generation of biocatalysts that are optimally adaptable to even demanding industrial process parameters. Such features form the fundaments of so-called white biotechnology – the use of microorganisms and enzymes for industrial chemical production, which currently strongly benefits from political support because of its impact on sustainable development, lower energy consumption and independence from fossil raw materials. Rising oil prices from a shortage of crude oil resources and political uncertainty in oil-producing countries; global warming due to greenhouse gases; increasing population; and environmental pollution are strong drivers for this trend.

Utilization of biocatalysis for chiral chemical synthesis and pharmaceutical manufacturing has come a long way, from highly specific niche applications a century ago, through hundreds of small to medium scale industrial processes in the fine chemical sector, e.g. including antibiotics, to even bulk processes for non-chiral commodity chemicals such as acrylamide. The conversion of traditional industrial processes to biotechnological alternatives is still at an early stage, because high costs in the development and adaptation of new processes have slowed down a substitution; development cycles for such biocatalytic processes used to be longer than anticipated and considerably longer than those for comparable chemical process alternatives. In the long run, however, biocatalytic processes have often

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proven to be economically feasible, ecologically advantageous and more sustainable than current chemical technologies because of the intrinsic advantages of biocatalysts in higher reaction selectivity, milder reaction conditions and potential use of inexpensive regenerable resources. After all, the tools of the trade have changed dramatically over the past decade, and with current advanced technology in protein design and engineering, further developments are expected to strongly gain momentum for the immediate future. As one of the most impressive examples, the newly developed one-step fermentation process for vitamin B_2 at BASF has cut CO_2 emissions by 30%, production costs by 40%, consumption of resources by 60% and waste generation by 95% when compared to the conventional eight-step chemical synthesis.

Still, the field of biocatalysis research for preparative synthesis poses a range of intellectual frontiers and needs further developments to broaden the range of applicable reaction types, addressable target structures and advanced method integration. There is both general and industrial interest in further research to extend the scope of biocatalysis for asymmetric synthesis, and a collaboration of organic chemists, biochemists, molecular geneticists and biotechnical engineers is needed for success. The development of biocatalytic methodologies undoubtedly requires strong interdisciplinary and transdisciplinary research cooperation, and meeting the challenges for an environmentally friendly, sustainable process design adds another dimension, from the supply and efficient use of raw materials to the minimization and recycling of enzymes, by-products and waste under economical constraints. This book summarizes the efforts and current state of the art in several important arenas of biocatalysis research that has been coordinated within the activities of the European Union-funded COST network D25, entitled 'Applied Biocatalysis: Stereoselective and Environmentally Friendly Reactions Catalysed by Enzymes', over the last five years. The topics of the chapters span from modern assay technologies for enzyme screening over different factors influencing enzyme selectivities, including the consequences from enzyme formulation and various solvent effects, to the manifold of preparative applications. More than half of the book chapters deal with the various conceptual strategies and synthetic opportunities available for the rational synthesis or targeted modification of different compound classes, such as phenolic natural products, nucleoside analogs, monosaccharides and oligosaccharides, iminosugars, proteinogenic and non-proteinogenic amino acids, nitriles, hydroxy acids, and various oxidation products, including lactones from enzymatic Baeyer–Villiger reactions.

We are grateful to all those friends and colleagues who helped to start, and then participated in, the D25 action and who kindly contributed to this project as authors of dedicated and informative chapters in order to share their expertise with you. It is our hope that this volume will encourage scientific discussion and foster imaginative new developments in applied biocatalysis for tomorrow's novel applications.

Wolf-Dieter Fessner and Thorleif Anthonsen
Darmstadt and Trondheim, October 2008

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ISBN: 978-3-527-32071-4

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ISBN: 978-3-527-32071-4