Biotransformations in Organic Chemistry

Kurt Faber

Biotransformations in Organic Chemistry

A Textbook

Seventh extended
and corrected edition

Springer

Kurt Faber
Department of Chemistry
University of Graz
Graz, Austria

ISBN 978-3-319-61589-9 ISBN 978-3-319-61590-5 (eBook)
DOI 10.1007/978-3-319-61590-5

Library of Congress Control Number: 2017944362

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

The use of natural catalysts – enzymes – for the transformation of nonnatural man-made organic compounds is not at all new: they have been used for more than 100 years, employed either as whole cells or isolated enzymes [1]. While the object of the early research was the elucidation of biochemical pathways and enzyme mechanisms, it was the steep rise of asymmetric synthesis during the 1980s that the enormous potential of enzymes for the synthesis of nonnatural organic compounds was recognized. What started as an academic curiosity in the late 1970s became a hot topic in synthetic organic chemistry in the 1990s. Driven by breathtaking developments in molecular biosciences, the search for novel enzymes, their production, and adaptation to industrial processes are continuously simplified, which is demonstrated by the wavelike appearance of novel biocatalytic principles. As a result of this extensive research, there have been an estimated 18,000 papers published on the subject to date. To collate these data as a kind of "super-review" would clearly be an impossible task, and, furthermore, such a hypothetical book would be unpalatable for the non-expert [2–5].

This textbook is written from an organic chemist's viewpoint to provide a *condensed* introduction into biocatalysis and to persuade synthetic chemists to think outside the box and to consider biocatalytic methods as an alternative tool for stereoselective synthesis. By this means, the wide repertoire of synthetic methods has been significantly widened and complemented, which is illustrated by the fact that the proportion of papers on asymmetric synthesis employing biocatalytic methods has constantly risen from zero in 1970 to about 8% at present. Certainly, biochemical methods are not superior in a general sense – they are no panacea – but they provide powerful tools to complement "chemical" methodology for a broad range of highly selective organic transformations. Synthetic chemists capable of using this potential have a clear advantage over those limited to nonbiological methods to tackle the new generation of synthetic problems at the interface between chemistry and biology, particularly in view of the necessity to use renewable feedstocks.

In this book, reliable biotransformations, which already had significant impact on organic chemistry, are put to the fore, including industrial-scale showcases.

Enzymes possessing great potential but still having to show their reliability are mentioned more briefly. The literature covered extends to spring 2017 and special credit is given to selected "very old" papers to acknowledge the appearance of novel concepts. The most useful references are selected from the pack, and special emphasis is placed on reviews and books, which are mentioned during the early paragraphs of each chapter to facilitate rapid access to a specific field if desired. After all, I tried to avoid writing a book with the charm of a telephone directory!

The first edition of this book appeared in 1992 and was composed as a monograph. It was not only well received by researchers in the field but also served as a basis for courses in biotransformations worldwide. In subsequent editions, emphasis was laid on didactic aspects in order to provide the first textbook on biocatalytic methods for organic synthesis, which served as a guide at several academic institutions for updating a dusty organic chemistry curriculum by incorporating biochemical methods. The need to account for the continuous emergence of novel enzymes and new protocols to use them prompted this updated and extended edition.

My growing experience in teaching biotransformations for organic synthesis at several universities and research institutions around the world has enabled me to modify the text of this seventh edition so as to facilitate a deeper understanding of the principles, not to mention the correction of errors, which escaped my attention during previous editions. I am grateful to numerous unnamed students for pointing them out and for raising tough questions.

I wish to express my deep gratitude to Stanley M. Roberts (UK) for undergoing the laborious task of correcting the first edition of this book. Special thanks go to Michael Müller, Martina Pohl, Wolf-Dieter (Woody) Fessner, (Germany), Nick Turner (UK), and Bernd Nidetzky (Graz) for their helpful hints and discussions. This revised edition would not have been possible without the great assistance of Wolfgang Kroutil for pointing out erroneous absolute configurations, Jörg Schrittwieser for discussing didactics, Georg Steinkellner for great enzyme pictures, and Melanie Hall for patiently answering my ignorant questions regarding molecular biology.

I shall certainly be pleased to receive comments, suggestions, and criticism from readers for incorporation in future editions.

Graz, Austria Kurt Faber
Spring 2017

References

1. For the history of biotransformations, see:
Neidleman SG (1990) The archeology of enzymology. In: Abramowicz D (ed) Biocatalysis, Van Nostrand Reinhold, New York, pp 1–24
Roberts SM, Turner NJ, Willetts AJ, Turner MK (1995) Introduction to Biocatalysis Using Enzymes and Micro-organisms, Cambridge University Press, Cambridge, pp 1–33

2. For monographs, see:

Jones JB, Sih CJ, Perlman D (eds) (1976) Applications of Biochemical Systems in Organic Chemistry, part I and II, Wiley, New York

Davies HG, Green RH, Kelly DR, Roberts SM (1989) Biotransformations in Preparative Organic Chemistry, Academic Press, London

Halgas J (1992) Biocatalysts in Organic Synthesis, Studies in Organic Chemistry, vol 46, Elsevier, Amsterdam

Poppe L, Novak L (1992) Selective Biocatalysis, Verlag Chemie, Weinheim

Roberts SM, Turner NJ, Willetts AJ, Turner MK (1995) Introduction to Biocatalysis Using Enzymes and Micro-organisms, Cambridge University Press, Cambridge

Bornscheuer UT, Kazlauskas RJ (2006) Hydrolases for Organic Synthesis, 2nd ed., Wiley-VCH, Weinheim

Bommarius AS, Riebel B (2004) Biocatalysis, Fundamentals and Applications, Wiley-VCH, Weinheim

Grunwald P (2009) Biocatalysis, Biochemical Fundamentals and Applications, Imperial College Press, London

3. For reference books, see:

Drauz K, Gröger H, May O (eds) (2012) Enzyme Catalysis in Organic Synthesis, 3rd edn, 3 vols, Wiley-VCH, Weinheim

Liese A, Seelbach K, Wandrey C (eds) (2006) Industrial Biotransformations, 2nd edn, Wiley-VCH, Weinheim

Hilterhaus L, Liese A, Kettling U, Antranikian G (eds) (2016) Applied Biocatalysis, Wiley-VCH, Weinheim, Germany.

Riva S, Fessner W-D (eds) (2014) Cascade Biocatalysis, Wiley-VCH, Weinheim, Germany.

P Grunwald (ed) (2015) Industrial Biocatalysis, Stanford, Singapore.

4. For a collection of preparative procedures, see:

Whittall J, Sutton PW (eds) (2010) Practical Methods for Biocatalysis and Biotransformations, Wiley, Chichester

Jeromin GE, Bertau M (2005) Bioorganikum, Wiley-VCH, Weinheim

Faber K, Fessner W-D, Turner NJ (eds) (2015) Biocatalysis in Organic Synthesis, in: Science of Synthesis, 3 vols Thieme, Stuttgart.

5. For the application of biotransformations to stereoselective synthesis, see:

Patel (ed) (2016) Green Biocatalysis, Wiley, Hoboken, NJ.

Tao J, Lin G-Q, Liese A (eds) (2009) Biocatalysis for the Pharmaceutical Industry, Wiley, Singapore.

Tao J, Kazlauskas R (eds) (2011) Biocatalysis for Green Chemistry and Chemical Process Development, Wiley, Hoboken, NJ.

Goswami A, Stewart JD (eds) (2016) Organic Synthesis Using Biocatalysis, Elsevier, Amsterdam.

Turner N (2017) Biocatalysis in Organic Synthesis: The Retrosynthesis Approach, RSC, London.

Contents

1 Introduction and Background Information 1
1.1 Introduction 1
1.2 Common Prejudices Against Enzymes 2
1.3 Advantages and Disadvantages of Biocatalysts 3
1.3.1 Advantages of Biocatalysts 3
1.3.2 Disadvantages of Biocatalysts 7
1.3.3 Isolated Enzymes Versus Whole Cell Systems 8
1.4 Enzyme Properties and Nomenclature 11
1.4.1 Structural Biology in a Nutshell 11
1.4.2 Mechanistic Aspects of Enzyme Catalysis 13
1.4.3 Classification and Nomenclature 20
1.4.4 Coenzymes 23
1.4.5 Enzyme Sources 25
References 26

2 Biocatalytic Applications 31
2.1 Hydrolytic Reactions 31
2.1.1 Mechanistic and Kinetic Aspects 31
2.1.2 Hydrolysis of the Amide Bond 49
2.1.3 Ester Hydrolysis 58
2.1.4 Hydrolysis and Formation of Phosphate Esters 104
2.1.5 Hydrolysis of Epoxides 115
2.1.6 Hydrolysis of Nitriles 124
2.2 Reduction Reactions 133
2.2.1 Recycling of Cofactors 134
2.2.2 Reduction of Aldehydes and Ketones Using Isolated Enzymes 140
2.2.3 Reduction of Aldehydes and Ketones Using Whole Cells 146

2.2.4 Reduction of C=N Bonds . . . 156
2.2.5 Reduction of C=C-Bonds . . . 161
2.3 Oxidation Reactions . . . 167
2.3.1 Oxidation of Alcohols and Aldehydes . . . 168
2.3.2 Oxidation of Amines . . . 171
2.3.3 Oxygenation Reactions . . . 173
2.3.4 Peroxidation Reactions . . . 198
2.4 Formation of Carbon–Carbon Bonds . . . 204
2.4.1 Aldol Reactions . . . 204
2.4.2 Thiamine-Dependent Acyloin and Benzoin Reactions . . . 218
2.5 Addition and Elimination Reactions . . . 224
2.5.1 Addition of Water . . . 224
2.5.2 Addition of Ammonia . . . 227
2.5.3 Cyanohydrin Formation and Henry-Reaction . . . 229
2.5.4 Michael-Type Additions . . . 233
2.6 Transfer Reactions . . . 235
2.6.1 Glycosyl Transfer Reactions . . . 235
2.6.2 Amino Transfer Reactions . . . 245
2.7 Halogenation and Dehalogenation Reactions . . . 250
2.7.1 Halogenation . . . 251
2.7.2 Dehalogenation . . . 256
References . . . 261

3 Special Techniques . . . 315
3.1 Enzymes in Organic Solvents . . . 315
3.1.1 Ester Synthesis . . . 325
3.1.2 Lactone and Lactame Synthesis . . . 343
3.1.3 Amide Synthesis . . . 344
3.1.4 Peptide Synthesis . . . 347
3.1.5 Peracid Synthesis . . . 353
3.1.6 Redox Reactions . . . 354
3.1.7 Medium Engineering . . . 356
3.2 Cascade-Reactions . . . 357
3.3 Immobilization . . . 369
3.4 Artificial and Modified Enzymes . . . 379
3.4.1 Non-Proteinogenic Enzyme Mimics . . . 379
3.4.2 Modified Enzymes . . . 379
3.4.3 Catalytic Antibodies and Computational De-Novo Design of Enzymes . . . 386
References . . . 389

4 State of the Art and Outlook . . . 407
References . . . 414

5 Appendix 415
5.1 Basic Rules for Handling Biocatalysts 415
5.2 Make Your Own Enzymes: Some Guidelines for the Non-specialist 418
5.3 Abbreviations 419
5.4 Suppliers of Enzymes 420
5.5 Major Culture Collections 421
5.6 Pathogenic Bacteria and Fungi 422

Index 423