Part II

Synthetic Applications

Introduction

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The ability to form esters and amides by condensation reactions, the absence of hydrolytic side reactions, the manipulation or regio- and stereoselectivity, and the advantages derived from high substrate and product solubilities have all contributed to continued investigation of the synthetic applications of enzymes in nonaqueous solvents. Methodology in this area has focused on the application of isolated enzyme catalysis under nonaqueous or low-water conditions, with free or immobilized enzymes operation in water-miscible solvent mixtures (e.g., methanol/water), water-immiscible solvents (e.g., hexane), and reverse micelle and encapsulated environments. Although water-miscible solvents are generally used only as a means to increase substrate solubility, water-immiscible solvents can also be used to alter and enzyme's reactivity.

Whole-cell biocatalysts can also be used in nonaqueous media, water/solvent two-phase systems, and reverse micelles. Such methods are particularly useful when dealing with the biotransformations of water-immiscible substrates that can act as the second phase (e.g., toluene), or for microbial conversions of those substrates possessing an appropriate partition coefficient between the two solvents. They are also valuable for biotransformations for which extensive cofactor recycling and thus cell viability is not a requirement, and for conversions involving microorganisms (such as Rhodococcus) that maintain high viability in the presence of organic solvents. In some instances, such as cases where competing enzymes may have different activities in a range of solvents, the nature of the solvent may also control the regio- or stereoselectivity of the biotransformation of a single substrate by whole cells.

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The contributions presented in this section cover a wide range of synthetic applications. The bulk of the work in this area has focused on the use of hydrolytic enzymes for the formation of esters and amides, and this is reflected in the following section, beginning with a discussion of the empirical rules available for the selection of such enzymes for enantioselective reactions. This is followed by a range of specific applications for the preparation of chiral alcohols by transesterification reactions using various lipase enzymes, together with an example of how such processes can be optimized for enantioselectivity. The selective formation of amides of amino-polyols is the presented, followed by a discussion of the use of lipases for esterification reactions in water–oil emulsions. Several reactions of water-insoluble organosilicon substrates catalyzed by hydrolytic enzymes are then discussed, followed by two contributions covering the use of a wider range of enzymes under a variety of conditions for hydrolytic and other reactions of multiple substrates types.

Whole-cell applications are exemplified by discussions of microbial reactions using an interface bioreactor, and of yeast-mediated reactions in organic solvents, and finally a case study of the development of a method for the preparation of the antifungal agent SCH56592 is presented, in which the use of nonaqueous biocatalysis is played a significant role.

The contributions in this section thus cover the scope of synthetic applications, from the initial concept of an idea and the choice of a suitable catalyst to the application of nonaqueous enzyme technology for chemical production.