ECONOMIC MICROBIOLOGY
Volume 5

MICROBIAL ENZYMES AND BIOCONVERSIONS

edited by

A. H. ROSE

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University of Bath,
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CONTRIBUTORS

KNUD AUNSTRUP, Novo Industri A/S, Novo Alle, DK-2880 Bagsvaerd, Denmark.

S. A. BARKER, Department of Chemistry, University of Birmingham, Birmingham, England.

J. ERIKSEN, Institute of Microbiology, University of Bergen, 5015 Bergen, Norway.

WILLIAM F. FOGERTY, Department of Industrial Microbiology, University College, Stillorgan Road, Dublin 4, Eire.

JOSTEIN GOKSØYR, Institute of Microbiology, University of Bergen, 5015 Bergen, Norway.

K. KIESLICH, Gesellschaft fur Biotechnologische Forschung mbH, D-3300 Braunschweig-Stockheim, West Germany.

W. PILNIK, Department of Food Science, Agricultural University, De Dreijen 12, 6703 BC Wageningen, Netherlands.

F. M. ROMBOUTS, Department of Food Science, Agricultural University, De Dreijen 12, 6703 BC Wageningen, Netherlands.

A. H. ROSE, School of Biological Sciences, University of Bath, Claverton Down, Bath, England.

OLDRICH K. SEBEK, The Upjohn Company, Kalamazoo, Michigan 4900, U.S.A.

J. SHIRLEY, Department of Biochemistry, University of Birmingham, Birmingham, England.

E. J. VANDAMME, Laboratory of General and Industrial Microbiology, University of Gent, Coupure 533, 9000-Gent, Belgium.

LEO C. VINING, Department of Biology, Dalhousie University, Halifax, Nova Scotia, Canada.

DR. DAVID PERLMAN

This volume of *Economic Microbiology* is dedicated to the memory of Dr. David Perlman (1920–1980).

Dr. Perlman received his doctorate from the University of Wisconsin where he studi d under Marven J. Johnson and William H. Peterson. After brief spells in the research laboratories of Hoffman–LaRoche Inc. and Merck and Co., he joined the Squibb Institute for Medical Research in New Brunswick, New Jersey, U.S.A. During his 20 years at Squibb, he developed several fermentation processes and his name will always be associated with streptomycin production, a fermentation in which he made a number of outstanding discoveries. Finally, Dr. Perlman moved back to the University of Wisconsin, as Professor of Pharmaceutical Biochemistry, where he also served as Dean of the School of Pharmacy.

Throughout his career, Dr. Perlman contributed regularly and richly to the literature on industrial microbiology. He has his name on 28 patents and more than 350 papers. His contribution to the review literature in fermentation science was especially powerful, most notably in his editorship of *Advances in Applied Microbiology* and, more recently, of *Annual Reports on Fermentation Processes*. Dr. Perlman had promised to contribute a short chapter to the present volume on conversions by *Gluconobacter* spp. Sadly, his last illness prevented this. He will be remembered as one of the great contributors to fermentation science.

A.H.R.

PREFACE

Production by microbiological processes of alcoholic beverages, and of a vast range of primary and secondary products of microbial metabolism, was covered in the first three volumes in this series. The fourth volume dealt with manufacture of microbial biomass, which in physiological terms can be viewed as production of cellular protein for use as food and fodder. All of the processes covered in these first four volumes exploit the metabolic idiosyncracies of micro-organisms for commercial use. The topics covered in the present volume differ from those described in the first four volumes of the series in that they are concerned with industrial exploitation not of entire metabolic pathways in microbes, but of individual enzymes or short sequences of enzymes.

Microbial enzymes have been used industrially for centuries, and until comparatively recently without any knowledge of the nature of enzymes. Commercial use of microbial enzymes received a tremendous fillip in the 1960s when proteases were incorporated into washing powders, and this did much to encourage further industrial use of microbial enzymes. The majority of microbial enzymes currently used in industry are extracellular depolymerizing or hydrolytic enzymes, but other classes of enzyme are beginning to find commercial uses, particularly in diagnostic kits. Additional uses for microbial enzymes are being actively researched in many countries of the World, and this constitutes one of the major growth areas in industrial microbiology.

In exploiting intact micro-organisms to carry out particular enzyme-catalysed reactions, or a chemical conversion that involves just a few enzymes, the industrial microbiologist is essentially using microbes as chemical reagents. The number of these processes operated com-

mercially is now quite large. This particular group of processes became widely known when microbes were first used to bring about structural alterations in steroid molecules, a breakthrough that greatly lowered the cost of cortisone production and, later, was extensively used in the manufacture of oral contraceptives. This too is a major growth area in economic microbiology, one closely allied with the chemical and pharmaceutical industries.

I am extremely grateful for the advice given to me during the preparation of this volume by my colleague Alan Rayner.

August, 1980 ANTHONY H. ROSE

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ANTHONY H. ROSE

School of Biological Sciences, University of Bath, Bath, Avon, England

I. INTRODUCTION

Commercial production of microbial primary and secondary products of metabolism, as well as of alcoholic beverages and biomass, involves

a highly co-ordinated series of enzyme-catalysed reactions which are associated with growth of the producing micro-organism. In addition, there are other industrially important microbiological processes which involve just one enzyme or a small number of enzymes. Where the process involves just one microbial enzyme, this can be extracted from cultures of the producing micro-organism, and used under conditions where the extent to which the substrate of the reaction is converted into product is under the more or less total control of the operator. Alternatively, activity of the enzyme—or there may be two or more—can be exploited using intact microbes, again under conditions that allow the operator to control the extent to which the substrate is converted into the desired product. In both types of process, the isolated enzyme or intact micro-organism is being used essentially as a chemical reagent to effect economically important molecular transformations. Individual chapters in this volume describe the more important of these enzymes and bioconversions.

II. HISTORY OF INDUSTRIALLY IMPORTANT MICROBIAL ENZYMES AND BIOCONVERSIONS

A. Enzymes

The concept of catalysis, the process by which the rate at which chemical reactions proceed is speeded up by the presence of another chemical compound that classically does not itself undergo chemical change, was developed rapidly in the early part of the Nineteenth Century. The first catalytic reaction described in the literature was the observation made by Vogel (1812) that, at low temperatures, oxygen and hydrogen react chemically when mixed in the presence of charcoal. Berzelius, a few years later in 1837, defined catalysis as a force apart 'such that material may, by their mere presence, and not on account of their chemical affinities, awaken in a substance such affinities as are latent at the temperature in question'; this translation comes from Keilin (1966). Presciently, Berzelius (1837) went on to assume that 'in living plants and animals, thousands of catalytic processes take place between tissues and fluids, thus giving rise to multitudes of chemical compounds'. Again, I am indebted to Keilin (1966) for this translation.