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FOREWORD

Organic synthesis has undergone a revolution over recent decades. Because the revolution has been a gradual one it has not been appreciated by many workers in other disciplines. However, organic synthesis underpins many other areas of science ranging from the development of designer polymers to molecular biology. Its very success has meant that organic synthesis is rarely the rate limiting step in investigations which depend on the availability of specific organic compounds. Workers in areas such as molecular biology and pharmaceutical science have got used to the idea that the compounds they need are available "off the shelf", without appreciating, perhaps, the enormous effort that has gone into developing the synthetic methods that have led, for them, to this happy state of affairs. However, in spite of the current advanced state of the art of organic synthesis, problems remain in certain areas that can introduce bottlenecks in otherwise efficient synthetic procedures. It is in some of these areas that biotransformations have an important role to play.

The application of enzymes in organic synthesis is not new. Examples can be found in the literature of more than a century ago. The upsurge in interest in biotransformations in the last ten to fifteen years has a number of origins. Among these, the increasing availability of enzymes, largely driven by commercial considerations that have nothing to do with organic synthesis, has played a major part. This is particularly evident in the growth of applications of lipases, most of which have been developed for use by the food and detergent industries. Organic chemists have been quick to seize on the opportunities opened up and have used lipases for many applications, particularly those having to do with the control of stereochemistry in organic synthetic sequences. This is particularly apparent in Part One of this special issue of *Tetrahedron: Asymmetry* which is devoted almost entirely to applications of lipases in the stereocontrol of organic transformations. Readers will note, however, that the range of lipases used is still small. Applications of the lipases from porcine pancreas, *Candida cylindracea* (*Candida rugosa*) and *Pseudomonas* species greatly outnumber the rest. What is astonishing is the range of compounds susceptible of transformation in reactions catalysed by these enzymes, a range that points to the fact that many more extremely useful enzymes, some known, some unknown, have unrealised possibilities that await exploitation. There are by now so many published applications of certain enzymes, including the lipases mentioned above and of other frequently used enzymes such as porcine liver esterase, that their applicability and characteristics (such as the stereochemistry of catalysed reactions) are rather predictable. However, the fact remains that enzymes nominally the same, but from different sources, often prove to have significantly different properties. This is sometimes attributable to the fact that often the preparations used are crude mixtures containing more than one catalytically active species. Progress in biotransformations, and particularly its wider acceptance as a legitimate and useful technique by the organic chemistry community, will be greatly advanced by fundamental studies of the mechanisms of enzymes of demonstrated usefulness, and by making them available in pure form, or at least in a form in which the useful enzyme is not accompanied by others also active on the substrates under investigation.

Redox reactions continue to play an important role in organic synthesis. The problems of recycling of cofactors, although largely solved, are still usually circumvented by the use of whole microorganisms. This is clearly revealed in Part Two of this special issue, which shows that baker's yeast still holds its position at the top of the league table of redox systems applied in biotransformations. Although this can be attributed in part to the

conservatism of organic chemists, it also reflects that fact that the yeast supplied to commercial bakeries has attributes that are demanded by organic chemists including ready availability, stability, reproducibility, consistent quality, robustness and low cost. For particular applications, even modest screening of available microorganisms can reveal strains that give better results with respect to yield or selectivity or both. Again, we can look forward to future developments in which many other strains of microorganisms come into more widespread and general use.

Carbohydrate chemistry is undergoing a strong renaissance, largely driven by the revelation of the crucial role of carbohydrates in many molecular recognition and signalling systems in living organisms. In this area, new methods are urgently needed. Although there have been enormous strides in carbohydrate synthesis, it remains a complex and time-consuming business. It is by now accepted that enzymatic methods have a significant role to play in this area and this is illustrated by contributions in Part Two of this special issue.

Oxygenases can often catalyse reactions that are difficult or impossible to carry out in the current state of the art of organic synthesis. This is particularly evident in the aromatic hydroxylating systems that give rise to homochiral products that have been widely exploited in natural product synthesis. Studies of the introduction of oxygen into sites lacking formal activation continue to be interest and are likely to expand, particularly in the absence of equivalent non-enzymatic processes. Papers illustrating progress in this area appear in Part Two.

The continued strong growth of biotransformations is illustrated by the enthusiastic response to invitations to contribute to this special issue, a response that has been so great that the issue has had to be produced in two parts. The steadily increasing numbers of published syntheses in which an enzymatic step is incorporated as a routine procedure show that biotransformations are becoming more and more accepted as a standard tool in organic synthesis. We hope that the papers in this special issue will further that trend.

Finally, we should like to thank all those colleagues whose work has contributed to the success of this special issue and express our appreciation to all who have submitted papers.

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