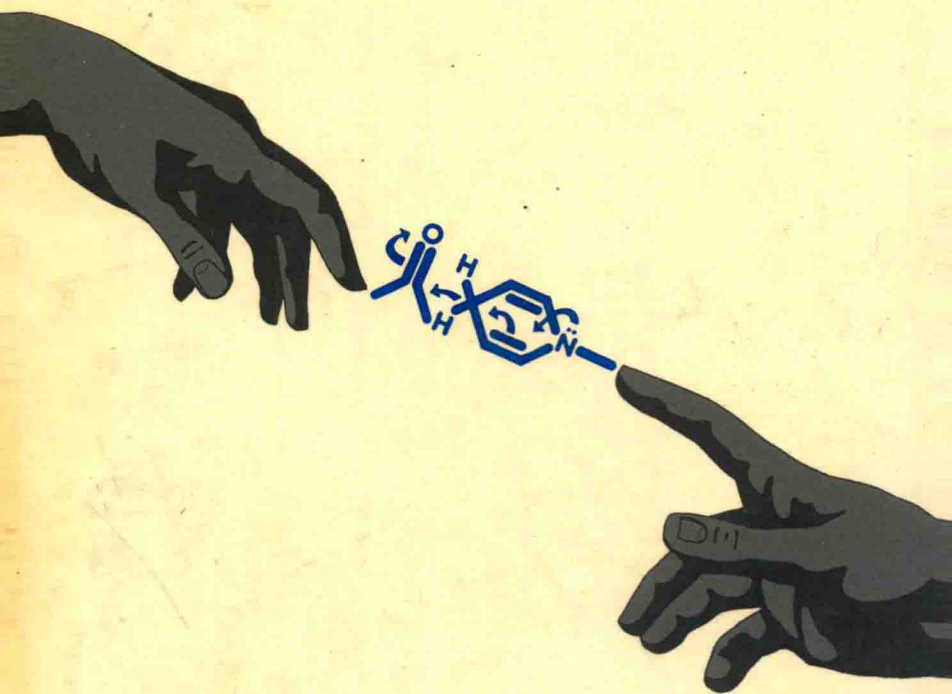


Enzyme Mechanisms

Edited by M.I. Page and A. Williams



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Enzyme Mechanisms

Preface

The chemistry of enzymes and enzyme-catalysed reactions is one of the major areas of overlap between chemistry and biology. Metabolic processes have a chemical logic which is only matched in its fascination by the logic of the reaction mechanism of a particular interconversion. There is no doubt that the elucidation of the mechanisms of catalysis by enzymes is enormously aided by studies of the mechanisms of simple organic reactions in solution; indeed, the study of enzyme mechanism is one part of an overall endeavour to understand the dynamics of reaction processes. Application of the techniques of physical organic chemistry to the study of enzyme-catalysed reactions has lead to an amazingly detailed picture of how bonds are made and broken in these processes. The direction of electron flow accompanying bond cleavage is often facilitated by stabilising forces that would be predicted by the experience gained in the study of regular organic reaction mechanisms.

Whereas a thorough description of enzyme mechanisms was at one time thought to be impossible and in any case of academic interest only, it is now clear that such information is necessary for the successful application of enzymes as catalysts in large scale synthesis, as biosensors and as targets for drug design. The pharmaceutical industry has been one of the leaders in realising that investigations of enzyme inhibition can be strongly advanced by an understanding of the reaction mechanism. Knowledge of enzyme mechanisms has inspired a growing body of active research on non-proteinaceous synthetic catalysts which may eventually be used industrially under conditions where enzymes decompose.

There is no implication here that 'catalytic- or active-sites' in enzymes are solely responsible for catalysis; a more apt description of this space would be the bond making and breaking site. The rate enhancement brought about by enzymes is often attributable to the stabilisation provided by the binding energy between the non-reacting parts of the substrate and the enzyme rather than by the actual chemical mechanism of bond-formation and fission. Nonetheless, a knowledge of the latter processes is required for, among other things, the design of mechanism based inhibitors and the possible 'tailoring' of an enzyme for it to catalyse reactions other than the 'natural' one.

The structure and activity of enzymes may be altered by manipulating their coding genes and the ability to replace specific amino-acid residues will undoubtedly further enlarge the picture of how enzymes discriminate between substrates and increase their rates of reaction.

We have been fortunate in having so many prominent research workers contribute to this volume; it is due to their enthusiasm if the book is favoured.

Michael I. Page, *Huddersfield*

Andrew Williams, *Canterbury*

1986

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