

# BIOORGANIC CHEMISTRY

*Edited by*  
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Stanford, California

## Volume I ENZYME ACTION

A treatise to supplement Bioorganic Chemistry:  
An International Journal

*Edited by*  
E. E. van Tamelen

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## Foreword

What is bioorganic chemistry? It is the field of research in which organic chemists interested in natural product chemistry interact with biochemistry. For many decades the natural product chemist has been concerned with the way in which Nature makes organic molecules. In the absence of any information other than that provided by structure, conclusions had necessarily to be derived from structural analysis. Broad groups of natural products could be recognized, such as alkaloids, isoprenoids, and polyketides (acetogenins), which clearly had elements of structure indicating a common biosynthetic origin. Indeed, for alkaloids and terpenoids, structural work was greatly helped by such biogenetic hypothesis. Similarly, after A. J. Birch had made an extensive analysis of polyketides, the repeating structural element postulated also helped in the determination of structure.

The alternative, and complement, to the above analysis is to consider the chemical mechanisms whereby the units of structure are assembled into the final natural product. For example, alkaloid structure can often be analyzed in terms of anion-carbonium ion combination. Also, the later stages of biosynthesis of many alkaloids can be analyzed by the concept of phenolate radical coupling. In polyisoprenoids the critical mechanism for carbon-carbon bond formation is the carbonium ion-olefin interaction to give a carbon-carbon bond and regenerate a further carbonium ion.

The analysis of natural product structures in terms of either structural units or mechanisms of bond formation has been subjected to rigorous tests since radioactively labeled compounds became generally available. It is gratifying that, on the whole, the theories developed from structural

and mechanistic analysis have been fully confirmed by *in vivo* experiments.

Organic chemists have always been fascinated by the possibility of imitating in the laboratory, but without the use of enzymes, the precise steps of a biosynthetic pathway. Such work may be called biogenetic-type, or biomimetic, synthesis. This type of synthesis is a proper activity for the bioorganic chemist and undoubtedly deserves much attention. Nearly all such efforts are, however, much less successful than Nature's synthetic activities using enzymes. It is well appreciated that Nature has solved the outstanding problem of synthetic chemistry, viz., how to obtain 100% yield and complete stereospecificity in a chemical synthesis. It, therefore, remains a major task for bioorganic chemists to understand the mechanism of enzyme action and the precise reason why an enzyme is so efficient. We are still far from the day when we can construct an organic molecule which will be as efficient a catalyst as an enzyme but which will not be based on the conventional polypeptide chain.

Much of contemporary bioorganic chemistry is presented in these volumes. It will be seen that much progress has been made, especially in the last two decades, but that there are still many fundamental problems left of great intellectual challenge and practical importance.

The world community of natural product chemists and biochemists will be grateful to the editor and to all the authors for the effort that they have expended to make this work an outstanding success.

DEREK BARTON  
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## Preface

Although natural scientists have always been concerned with the development and behavior of living systems, only in the twentieth century have investigators been in a position to study on a molecular level the intimate behavior of organic entities in biological environments. By mid-century, the form and function of various natural products were being defined, and complex biosynthetic reactions were even being simulated in the nonenzymatic laboratory. As the cinematographic focus on biomolecules sharpened, one heard increasingly the adjective *bioorganic* applied to the interdisciplinary area into which such activity falls.

In 1971, publication of a new journal, *Bioorganic Chemistry*, was begun. As a follow-up, what could be more timely and useful than a well-planned, multivolume collection of bioorganic review articles, solicited from carefully chosen professionals, surveying the entire field from all possible vantage points? This four-volume work contains a collection, but it did not originate in this manner.

As the journal *Bioorganic Chemistry* developed, the number and quality of regular, original research articles were maintained at an acceptable level. However, comprehensive review articles appeared only sporadically, despite their intrinsic value at a time when general interest in bioorganic chemistry was burgeoning. In order to enhance this function of the journal, as well as to mark the fifth anniversary of its birth, we originally planned to publish in 1976 a special issue comprised entirely of reviews by active practitioners. After contact with a handful of stalwart bioorganic chemists, about two hundred written invitations for reviews were mailed during late 1975 to appropriate, diverse scientists throughout



the world. The response was overwhelming! More than seventy preliminary acceptances were received within a few months, and it soon became evident that the volume could not be handled adequately through publication by journal means. After consultation with representatives of Academic Press, we agreed to publish the manuscripts in book form.

Although the stringency of journal deadlines disappeared, the weightier matter of editorial treatment had to be reconsidered. Should contributions be published in the same, piecemeal, random fashion as received? Such practice would be acceptable for journal dissemination, but for book purposes, broader, more orderly, and inclusive treatment might be desirable and also expected. Partly because of editorial indolence, but mostly because of a predilection for maintaining the candor and spontaneity which might be lost with increased editorial control, we decided not to attempt coverage of all identifiable areas of bioorganic chemistry, not to seek out preferentially the recognized leaders in particular areas, and even not to utilize outside referees. Consequently, we present reviews composed by scientists who were not coerced or pressured, but who wrote freely on subjects they wanted to write about and treated them as they wanted to, at the cost perhaps of a certain amount of objectivity and restraint as well as proper coverage of some important bioorganic areas.

We turn now to the results of this publication project. Because of the inevitable attrition for the usual reasons, fewer than the promised number of reviews materialized: fifty-seven manuscripts were received in good time and accepted by this office. Eight countries are represented by the entire collection, which emanates almost entirely from academia, as would be expected. A great variety of topics congregated—greater than we had foreseen. Inclusion of all papers in one volume was impractical, and thus the problem arose of logically dividing the heterogeneous material into several unified subsections, each suitable for one volume, a problem compounded by the fact that an occasional author elected to treat, in one manuscript, several unconnected topics happening to fall in his purview. Therefore, perfect classification without discarding or dissecting bodies of material as received was simply not possible.

After some reflection and a few misconceptions, we evolved a plan for division into four more or less scientifically integral sections; these, happily, also constitute approximately equal volumes of written material, an aspect of some importance to the publisher. The enzyme-substrate interaction was expected to be a well-represented subject, and, in fact, too many manuscripts on this subject for one proportionally sized volume were received. Although the separation of enzyme action and substrate behavior is contrived and not basically justifiable, it turned out that, for the most part, a group of authors heavily emphasized the former, while another concentrated on the latter. Accordingly, Volume I was entitled

“Enzyme Action,” and Volume II “Substrate Behavior.” Admittedly, in a few cases, articles could be considered appropriate for either volume.

A gratifyingly significant number of contributions dealt with the behavior of biologically important polymers and related matters, sent in by authors having quite different investigational approaches. In addition, several discourses were concerned with molecular aggregates, e.g., micelles. All of these were incorporated into Volume III, “Macro- and Multimolecular Systems.”

Whatever papers did not belong in Volumes I–III were combined and constitute Volume IV. Fortunately, in these remaining papers some elements of unity could be discerned; in fact, their entire content falls into the following categories: “Electron Transfer and Energy Conversion (photosynthesis, porphyrins,  $\text{NAD}^+$ , cytochromes); Cofactors (coenzymes,  $\text{NAD}^+$ , metal ions); Probes (cytokinin behavior, steroid hormone action, peptidyl transferase reactivity).”

Finally, early in this enterprise, we asked Derek Barton to compose a Foreword. Sir Derek complied graciously, and in every volume his personalized view on the nature of bioorganic chemistry appears.

E. E. VAN TAMELEN

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