Foreword

Amino acid-derived compounds, as modified or linear peptides, continue to have a high impact in research as well applied sciences, as in pharmacy. This impact can be traced to a number of unique properties. Most important, these compounds contain a linear sequence of amino acids, that permits easily sequence variations in the study of structure-activity relations. The enzymology of peptide formation is well advanced, and applications of enzymes in production processes are emerging. A more detailed knowledge of the cellular targets permits new screening approaches and more extensive chemical variation studies. Such knowledge is intimately connected to the advancement of biochemistry, also made possible with the application of bioactive peptides as research tools.

In this monograph we have assembled major lines of research of the past years, that in each case has reached a certain level of completion. By this we provide an overview of the current directions of the field, that should provide a useful orientation for running projects as well as those to be planned. Current developments in fast moving projects have been included in an introductory chapter. Here we summarize aspects of biosynthesis of peptides formed by ribosomal and nonribosomal pathways, as well as compounds recently detected in new sources or by their unusual effects. Especially important is the progress made in the analysis and cloning of enzymatic pathways, such as β-lactam biosynthesis. This as a rapidly developing field is discussed here together with the advances in cloning of peptide synthetases. The best known multienzyme system, the gramicidin S synthetase, has been treated by Joachim Vater. A more general approach in the multienzymic field is given by Andreas Billich and Rainer Zocher on N-methylated peptide bonds, a feature very common in cyclic structures, and contributed by an integrated methylase function within multienzymic synthetases. A general consideration of enzymatically catalysed peptide bond formation is carried out by Volker Kasche and Günther Michaelis. Their conclusions already have found applications in synthetic chemistry of enzymic acylation reactions. For the genetics of an enzymic pathway Volkmar Braun gives a description of siderophore systems, as models for peptide bond containing metabolites.

Turning then to the more structural aspects, the following five chapters summarize work on the elucidation of structures and effects, the application of screens, and chemical modification studies in structure-function work. Hideo Ono and Setsuo Harada present an overview of the results of their screening for new β-lactams and β-lactam like antibiotics. Giancarlo Lancini and Bruno Cavalleri give an account of the extensive search for D-analyl-D-alanine binding glycopeptides of the vancomycin type. Phytotoxic peptides are reviewed by Jonathan Walton representative for the many highly toxic peptides frequently discovered by their ecological impact. The structural variation of antibiotics, a key problem in compound development, has been over the years most extensively executed with cyclic peptides of the gramicidin S type. This work is considered in perspective by Michinori Waki and

Nobuo Izumiya. A highlight in synthetic peptide chemistry has been the total synthesis of the potent immunomodulator cyclosporin. Now, as the structural work is in a more advanced state, Roland Wenger and Hans Fliri describe the chemical and biochemical implications in detail.

The following two chapters are devoted to Hamao Umezawa's school pioneering in the introduction of peptides as modulators of enzyme activity, with vast implications in disease treatment. Tomohisa Takita and Yasuhiko Muraoka summarize the work on biosynthesis and total synthesis of bleomycin, a highly complex glycopeptide, from which by extensive screenings useful derivatives for cancer chemotherapy have been developed. Takaaki Aoyagi, who has introduced numerous microbial proteinase inhibitors, focuses on the biochemical studies, that provide a basis for possible pharmacological applications.

The final contributions are concerned with the production of peptides. The structural variation of peptides by amino acid exchange upon substrate feeding has been investigated for neoviridogrisein by Yasushi Okumura. Immobilization of biocatalysts, a key step in commercial production processes, has been reviewed by Erick Vandamme.

As an appendix, a table of well characterized compounds has been compiled, arranged according to their structural properties, with some notes on their biochemical actions. This approach of compilation, that we have suggested earlier, should aid the researcher in the selection of comparable compounds, and permit search for structural homologies.

We are indebted to all our colleagues participating in this project, who took the burden of again presenting results and evaluating their fields in perspective. We are sure that this book will be a valuable tool for those working in the peptide field trying to correlate chemistry and biochemistry at various levels of application. We also thank the publishers for their interest and support.

Berlin, January 1990

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