Introduction to

MODERN BIOCHEMISTRY

P. Karlson

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by

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FOREWORD

Biochemistry is growing rapidly. No other branch of science has so deepened our grasp of fundamental life processes and so directly influenced the thinking and practice of physicians in recent decades. Its triumphal success with the chemistry of vitamins and hormones has been followed by an experimental attack on the constitution and mechanism of action of enzymes. Basic insight has been gained into the dynamic events of metabolism, so characteristic of every living cell. Understanding has also been gained regarding the production, conversion, and utilization of energy and of the ways in which cellular material is built up and broken down. We in our times have been permitted the first glimpses of the structure and mode of action of hereditary factors, which predetermine the biologic fate of cells.

This brief textbook of biochemistry by Peter Karlson, Professor of Physiological Chemistry at the University of Munich, attempts to organize the vast material according to the new viewpoints and with particular regard for current problems. For the students of medicine or natural science this textbook attempts to supplement the introductory courses in biochemistry and to close a gap existing in our biochemical literature. This book has evolved through our joint effort, over the years, to teach physiological chemistry. first in Tübingen, and now in Munich. I have the impression this book will fulfill its purpose, and with the author I hope that it may prove to arouse interest in the problems and importance of biochemistry and to motivate a deeper study of it.

ADOLF BUTENANDT

PREFACE

Modern biology has extended its analysis of life into molecular dimensions. In this region, the borderlines between the classical disciplines of morphology, physiology, and biochemistry are fading. Morphology is becoming the chemistry of structural elements—large molecules are now visible in the electron microscope; physiology is turning into the study of changes in the structural elements, which is also biochemistry; and "molecular biology," a new discipline, originates to a great extent in biochemistry.

There seemed to be a need for a concise book giving an introduction to biochemistry and a survey of the main facts and ideas. It is hoped that the American edition, translated from the third German edition (1962), will be favorably received and will fulfill its purpose, i.e., to provide a better understanding of the chemical background of biologic phenomena.

The material has been arranged according to didactic needs. Though many textbooks begin with carbohydrates, this seemed to be inappropriate, since the chemistry as well as the biochemistry of carbohydrates is rather complicated. Therefore we begin with simple compounds like amino acids (the introductory chapter on organic chemistry is mainly a short compendium of some relevant facts), and then turn to proteins and to enzyme proteins, leaving the carbohydrates for a later chapter. No distinction has been made between "descriptive biochemistry," the chemistry of natural products, and "dynamic biochemistry" or metabolism. On the contrary, in some chapters the chemical structures of the natural compounds have been deduced from the description of their biosyntheses.

In the selection of the material, biochemistry has been regarded as part of the science of life. Concepts of general importance, such as the generation and utilization of free energy, the role of genes in protein and enzyme synthesis, and the importance of the submicroscopic structure of the cell in biochemical reactions, have been emphasized in various places. Clinical problems have been treated only insofar as they have contributed to the knowledge of normal biochemistry; for a detailed discussion of pathologic biochemistry, the reader should refer to other textbooks.

It was impossible to include, in a short book, all the experimental proofs for the facts to be described. Also, no attempt was made to cover the methodology of biochemistry; only some newer methods have been mentioned, just to show, in a few examples, how the results have been obtained.

The numerous figures and formulas skillfully drawn by Josef Paland for the German edition are reproduced here also. My thanks are due to several colleagues for electron micrographs, to Dr. C. E. Doering for the translation of the text, and to Academic Press for the production of the volume.

Munich
March 1963

PETER KARLSON

ERRATA

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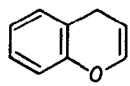
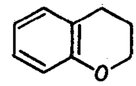
3	Table I	 Chroman	 Chroman
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104	12	Fig. *22d*,	Fig. 25d,
107	11	Fig. 22	Fig. 25
130	7	molecule *c*	molecules
136	18	Fig. 45	Fig. 48
137	24 and 25	Fig. 22	Fig. 25
142	6	bacteria	a mold
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190	3	potential (0.115 volts).	potential (−0.115 volts) than the cytochromes.
230	7	Sphingosine	Sphingomyelin
235	8	catalyzed . . . proceeds via	catalyzed double bond shift of a Δ^3- to a Δ^2-compound, and then proceeds *via*
239	11 and legend of formula	coprosterol	coprostanol
254	15	carboxy acids,	carboxylic acids,
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INTRODUCTION

Biochemistry is one of the life sciences. Its object is to study the phenomena of life by chemical methods.

The first requirement for this study is a knowledge of the chemical nature of cell components, an area commonly called "descriptive biochemistry"; it coincides in great part with the "chemistry of natural products." Organic chemistry nowadays is synonymous with the chemistry of carbon compounds, but in its beginning it was the chemistry of natural products; the purification and investigation of naturally occurring substances was its domain, whereas synthetic organic chemistry has developed since Wöhler's synthesis of urea, at first slowly, and then explosively, at times to the extent of repressing interest in natural products. In recent decades, interest has turned more and more toward high molecular natural products. The determination of the constitution of proteins and nucleic acids is at present the most important problem of descriptive biochemistry.

The pure description of chemical substances can, however, offer only a static picture, a snapshot of the living cell (or of a living organism), and cannot cope with the problem of investigating the *phenomena of life*. The fascinating dynamic activities of the living cell, its unceasing changes, are the proper characteristics of life, and the study of the chemical conversions constantly occurring there is the subject of "dynamic biochemistry." We know today that almost all substances built up by the cell are always in a state of turnover. Life is characterized by chemical motion, and what in the past appeared to be a static framework has now become part of its chemical activity.

Modern biochemistry, therefore, is primarily dynamic biochemistry. This includes first of all the various features of metabolism, namely, conversion and degradation of foodstuffs to gain chemical energy and to synthesize endogenous material. All these reactions are catalyzed by particular enzymes, whose study quite naturally occupies a large area in biochemistry.

The second aspect of dynamic biochemistry is chemical regulation. This may be achieved by certain metabolic products; often it is accomplished by special substances called hormones which are produced in endocrine glands.

Third, dynamic biochemistry is concerned with all those chemical processes that take place on the structural elements and that represent their real function. At this point there are close ties to physiology, another one of the "life sciences." Since structures are chemical entities, changes of structure are biochemical reactions. Thus biochemistry is prepared to provide explanations for physiological processes. Indeed, the analytical approach to biochemistry penetrates far more effectively than the physiological approach. Starling has said that every physiological problem ultimately is reducible to a biochemical one.

The chemical methodology employed by biochemistry has already provided some insight into the true nature of cellular activity. But, on the other hand, this approach does have definite limitations. When we use chemical methods we expect answers only from the field of chemical knowledge and experience. Phenomena of life belonging to other areas of science, as for example bioelectric properties, reaction to stimuli, and behavior, of course, cannot be approached by chemical methods; more suitable research methods are needed. Some phenomena, like man's consciousness, would appear to be entirely improper subjects for scientific analysis.

Just as biochemistry approaches problems in a variety of ways, so have its answers found application in a number of allied sciences. As far as medicine is concerned, many diseases are now recognized to be metabolic disturbances or biochemical anomalies, and obviously every drug, being a chemical substance, affects biochemical systems. To the medical man in particular, therefore, biochemical knowledge is simply indispensable.

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CHAPTER I

Organic Chemistry and Biochemistry

Biochemistry concerns carbon compounds and their reactions as they occur in organisms. Organic chemistry, or the chemistry of carbon compounds, therefore, is basic to biochemistry. The chemistry of natural products and that of biochemistry overlap extensively and lack a clearly defined border. Numerous compounds which have only recently been identified as intermediates of metabolism had long been known in organic chemistry.

A good knowledge of organic chemistry, in particular a thorough appreciation of structural formulas, therefore, is a prerequisite for an intelligent study of biochemistry. The following brief outline is not intended to replace a course in organic chemistry, but rather to serve as a handy reference for selected compounds and for reactions of special significance in biochemistry.

1. Hydrocarbons as Parent Substances

The great variety of organic compounds may be explained by the ease with which carbon atoms can attach to each other. Since carbon is tetravalent, a great many possibilities for branching arise, leading to a staggering number of carbon skeletons. If the remaining valence bonds are filled with hydrogen, then we speak of the result as a hydrocarbon. From a systematic viewpoint, hydrocarbons are the parent substances of all organic compounds; in practice, however, they are very rarely used to prepare other classes of compounds.

The molecular formulas of all saturated open-chain hydrocarbons are represented by the general formula C_nH_{2n+2}. Every time an open chain closes to a ring, irrespective of size of the ring, two hydrogen atoms are lost with a corresponding change in the general formula. Thus it becomes possible to deduce from the molecular formula of a saturated hydrocarbon such as cholestane, $C_{27}H_{48}$ (parent substance of cholesterol), that there must be four rings in its carbon skeleton.

Saturated or alicyclic ring systems actually are of equal if not greater importance in biochemistry than aromatic compounds derived from benzene, which dominate