



Biological Chemistry

An Introduction to
Biochemistry

GERO

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DEDICATION

To Wolfgang Pauli

PREFACE

A borderline can be approached from two sides, and biochemistry, a borderline science, can be presented from either the biological or the chemical viewpoint. So far the biological point of view has been dominant in all texts dealing with the subject.

In the present text, the emphasis is on the chemical approach, for which there are quite logical reasons. From conversations and correspondence with teachers of physiological chemistry at an advanced level, I gained the conviction that overemphasis on the biological approach does not provide the best possible equipment for the undergraduate student preparing for medical or dental school or for graduate studies in the sciences. Almost unanimously, medical schools deplored college courses in biochemistry as unnecessary duplication of subject matter studied in the medical school; but at the same time they were equally unanimous in calling for more thorough training of undergraduate students in organic and physical chemistry.

Trying to meet these demands, this text is essentially a somewhat advanced organic chemistry with special accent on that material most pertinent to the subsequent study of physiological chemistry. It is a revision and expansion of a mimeographed text, written in the hope that other teachers and students might find such an approach useful. The response of my students to this material, and their later performance in medical and graduate school, certainly has been most gratifying.

It is perhaps not necessary to emphasize that in writing this book I had only one preoccupation: the student. This is a textbook and nothing else. Its aim is to help the student who has had no more chemical experience than a year of general, a year of organic, and—at most—a year of analytical chemistry, to understand better some pertinent points in this sometimes difficult subject and to give him a secure foundation for his later more advanced work in biochemistry. The guiding principle is therefore clarity and simplicity in fundamentals—even oversimplification where it helps understanding—rather than completeness in details. At the same time I have attempted to fill in some of the painful gaps often left for lack of time in an elementary organic chemistry course, such as the subjects of optical activity, chemistry of heterocycles, etc.

It is impossible to be prepared for a study of physiological chemistry without some familiarity with physical chemistry. In recognition of this fact many colleges offer courses in physical chemistry specifically for premedical

students. However, this practice is not yet general and I could not assume all my readers to be sufficiently familiar with physical chemistry. Therefore the book begins with two chapters containing a brief and elementary summary of those principles of physical chemistry which are necessary for an understanding of biochemistry. They are written, with as simple mathematics as possible, for the student entirely unfamiliar with physical chemistry. The reader who feels at home in this science may safely ignore these chapters.

The third chapter likewise summarizes some results of the electronic theory of organic chemistry. While this topic is treated adequately at most colleges, some readers may feel the need for such a brief summary. Chapter 3 was written for their benefit.

Chapter 4 discusses optical activity, a topic of such tremendous importance for biochemistry that it deserves more than the hasty treatment it usually gets in elementary organic chemistry courses.

Chapters 5, 6, and 7 treat the topics underlying the chemistry of proteins, carbohydrates, and lipides, respectively. I have tried to discuss acids, amines, amides, amino acids, alcohols, ketones, esters, etc., adequately and was content to be rather sketchy about the proteins, carbohydrates, and lipides themselves. This is in keeping with the purpose of the book.

Chapters 8 and 9 deal with steroids and isoprenoids, important subjects for biochemistry but stepchildren of most elementary organic chemistry courses.

Chapter 10 includes a theoretical treatment of aromaticity and a survey of a number of aromatic compounds of biological or medicinal significance.

Chapter 11, "Heterocycles," attempts to supply information on a subject which graduate schools expect their students to bring along from college but which all too many colleges leave to graduate school. Besides general information, a number of important heterocyclic compounds—hemin, alkaloids, nucleotides—are discussed specifically.

Only one chapter, the twelfth, is devoted to outright biochemistry. Even here I have tried to emphasize the chemical rather than the biological approach, and the reader will find many references to hydration, oxidation, the Knoevenagel condensation, heats of reaction, activation energies, and other purely chemical topics, but none to liver slices or nutritional requirements. This, I feel, is the proper domain of medical or graduate school and should be omitted from a textbook written for undergraduate students.

Chapter 13, "Chemical Structure and Physiological Activity," may trespass on graduate terrain. But I believe that this is a subject of such great significance to the biologically interested chemistry student that something would be lacking if it were not included.

The following two chapters show the scientist at work, unraveling structures and reaction mechanisms and synthesizing biologically important complex structures. Much of this will no doubt appear dull and abstruse

to most of my readers but it is hoped that a few may be stimulated and inspired by the deeds of the great men of science reported here.

In keeping with the character of this book as a textbook, literature references in the text were avoided. Yet I can hope for no greater satisfaction than to generate in its readers an urge to learn more about the many fields it touches all too briefly. Therefore, in the last chapter I have assembled a list of books which are recommended for further reading.

I do not want to close this preface without thanking those who helped this textbook to materialize. I am especially indebted to my friend Professor F. C. Strong for many illuminating discussions and criticism of the two chapters on physical chemistry; to Dr. Linus Pauling, Dr. J. C. Sheehan, Dr. R. B. Woodward, Dr. J. M. Buchanan, Dr. Maximilian Ehrenstein, and Dr. M. D. Gates for having helped me with information on their recent researches; to the staff of The Blakiston Company, Inc., especially to Miss Laura E. Moore, Manuscript Editor, for good-humored patience and untiring advice; and to Villanova College, where I gained the experience which took shape in this book, for manifold help and encouragement.

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CHAPTER 1

SOME ELEMENTS OF PHYSICAL CHEMISTRY, I

1.1. Introduction. Importance of free-moving molecules. If it is true that most of the reactions of chemistry occur in solutions, this is even more true for the chemical reactions occurring in living organisms. Protoplasm, the prime living substance, consists of a complicated mixture of materials dissolved in water; blood, digestive fluids, lymph, or mucus are no less solutions than fruit juices, tree saps, rubber latex, or the nectar of blossoms. It is assuredly true if we say that life proceeds in solutions and that without solutions there is no life.

Now what characterizes solutions generally is the free mobility of the solute particles. In a solid piece of matter, the atoms and molecules of which it is composed are held rather rigidly in certain definite positions around which only oscillations of a limited amplitude are possible. In liquid matter, the elementary particles can slide past each other easily but their distance from each other is strictly maintained—liquids are neither compressible nor expansible.

But the molecules of the solute in a solution are practically independent of each other. They move around freely and can fill the entire volume of the solution, no matter how far they get from each other in the process. In this they are similar to the molecules of gases. As a result, the formulations which describe the behavior of gases are largely applicable also to solutions.

1.2. Gas laws. Boyle's Law. These formulations, known as the *gas laws*, are important to biochemistry also for another reason. The body is in constant equilibrium with its surroundings, notably with the atmosphere. This atmosphere consists of gases among which nitrogen, oxygen, and carbon dioxide are preëminent. The latter two are of fundamental importance for life processes; it is therefore of great concern to biochemistry to know how these gases interact with the solutions in which the chemical processes of the organism are carried out.

Because of the fundamental importance of the gas laws, it is customary to place them at the beginning of any study of physical chemistry. They state certain empirical facts about the behavior common to all gases.

First, *Boyle's Law* states that a given amount of gas—any gas—if kept at a constant temperature, will display a pressure inversely proportional to the volume it is allowed to occupy. That is, if a given amount of gas is at first in equilibrium with the atmosphere and is then compressed into half its original volume, its pressure will now amount to 2 atmospheres; it will be

3 atmospheres if the gas is compressed into one-third its original volume, but one-half atmosphere if, instead of being compressed, the gas is allowed to expand to twice its former volume, etc. In brief, we might describe the behavior of the gas by saying that it tends to dilute itself as much as possible and will resist any opposition to this tendency by pressing against the walls of any container in which it is imprisoned, the pressure being the greater the narrower the prison. When we change the volume of the gas, its pressure therefore changes too, in such a manner that the one always increases as many times as the other decreases. In mathematical shorthand,

$$P = \frac{K_1}{V} \quad (1)$$

$$\text{or} \quad PV = K_1 \quad (1a)$$

$$\text{or} \quad V = \frac{K_1}{P} \quad (1b)$$

wherein P signifies the pressure of the gas, V its volume, and K_1 a proportionality factor whose magnitude depends on the particular situation (amount of gas, initial pressure and volume, temperature) with which we have chosen to start.

1.3. Charles' Law. To this first statement on the behavior of gases at constant temperature, *Charles' Law* adds a second one referring to a change in temperature. It states that the volume of a given amount of gas, at constant pressure, varies in proportion to the absolute temperature. (We may recall that the absolute temperature scale, symbolized by K , is a centigrade scale counted from -273°C as the zero point. Therefore $0^\circ\text{C} = 273^\circ\text{K}$, $100^\circ\text{C} = 373^\circ\text{K}$, etc.)

If a gas, at a given pressure, occupies 273 ml of space at 0°C , it will therefore expand to 373 ml at 100°C , provided the pressure is kept constant. The mathematical formulation is

$$V = K_2 T \quad (2)$$

or

$$\frac{V}{T} = K_2 \quad (2a)$$

(The absolute temperature usually is indicated by a capital T .)

1.4. Gay-Lussac's Law. How the pressure depends on the temperature (*Gay-Lussac's Law*) follows from a combination of the laws of Boyle and Charles. Let us imagine an amount of gas which is heated and at the same time allowed to expand so that its pressure does not change. Then by the time it has been heated to twice its original (absolute) temperature it will also have expanded to twice its original volume, according to Charles' Law. Now we stop heating and, taking care to keep the new higher temperature constant, compress the gas to its original volume which—as we just found—is half its new volume. This, according to Boyle's Law, doubles its

pressure; generally, if the volume of a gas is constant, its pressure varies in proportion to the variation of the absolute temperature. The mathematical form of Gay-Lussac's Law is therefore entirely analogous to Charles' Law; it reads

$$P = K_3 T \quad (3)$$

or

$$\frac{P}{T} = K_3 \quad (3a)$$

1.5. General gas law. A *general gas law* would show how a gas responds to changing temperature when neither its volume nor its pressure is kept arbitrarily constant. It is possible to derive such a law from Boyle's and Charles' Laws. To this end let us imagine a gas which in its original state, at the temperature T_0 and the pressure P_0 , occupies the volume V_0 . Then let us further assume that, without changing the temperature, we compress the gas to the pressure P_1 . What now will be the volume to which the gas has been reduced? Boyle's Law gives the answer since we kept the temperature constant: the volume of the gas is inversely proportional to its pressure (Eq. 1b) and therefore the new volume V_0^1 is determined as

$$V_0^1 = \frac{K_1}{P_1} \quad (4)$$

Now let us heat the gas while keeping its pressure constant at P_1 . Charles' Law applies to this process and states that the volume will change with the temperature so that $\frac{V}{T}$ remains constant (Eq. 2a). By the time the temperature T_1 has been reached, our gas has expanded to a new volume V_1 , and, because of the constancy of $\frac{V}{T}$, the quotient $\frac{V_1}{T_1}$ (after the heating) must still be the same as the quotient $\frac{V_0^1}{T_0}$ (before the heating).

Let us express the intermediate volume V_0^1 so that only terms taken from the initial and final states appear in our equations. As we stated before,

$$V_0^1 = \frac{K_1}{P_1}$$

or $P_1 V_0^1 = K_1 = P_0 V_0$ (Boyle's Law, Eq. 1a); therefore, dividing both sides by P_1 ,

$$V_0^1 = \frac{P_0 V_0}{P_1}$$

and our further statement

$$\frac{V_1}{T_1} = \frac{V_0^1}{T_0}$$

may then be stated as

$$\frac{V_1}{T_1} = \frac{P_0 V_0}{P_1 T_0}$$