

represent a marked improvement over the usual physical chemistry text treatment in either approach or standard, but does provide a short and elementary approach to kinetics.

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Organophosphorus Poisons. Anticholinesterases and Related Compounds. By D. F. HEATH, Toxicology Research Unit, Medical Research Council Laboratories, Carshalton, Surrey. Pergamon Press Ltd., Headington Hill Hall, Oxford, England. 1961. vii + 403 pp. 16 × 23.5 cm. Price, \$12.50.

This book is volume 13 in the Modern Trends in Physiological Sciences Division of the International Series of Monographs on Pure and Applied Biology. In his preface, the author states that he has tried to make a multidisciplinary presentation of organophosphorus compounds that will be of value both to the expert in one subject who desires to understand the research in another closely related field and to the tyro in all fields. The author's approach to these two ends can be seen by an examination of the structure of his book.

The book starts with an Introductory Chapter, which really is a summary of the entire book. This chapter occupies the first 14 pages of the volume. Thereafter follow in order sections entitled Chemistry, Biochemistry, Pharmacology in Mammals and Pharmacology in Insects. Each of these sections contains one or more appropriate chapters. The text ends on page 353. An appendix on the Theory of Reaction Rates in Solution is followed by a Glossary of common names, systematic names and structural formulas for organophosphorus compounds. The final 29 pages of the book are occupied by subject and formula indices.

The chemistry section of the book contains discussions of nomenclature for organophosphorus compounds, of the electronic theory of reactions (with particular reference to nucleophilic replacement reactions), of synthetic methods for making various types of organophosphorus molecules, of methods for purifying the reaction products and of reactions between organophosphorus molecules and other organophosphorus molecules or other types of substances (with reference particularly to hydrolytic actions).

The section on Biochemistry begins with an account of various enzymes that react with the organophosphorus anticholinesterases, either being inhibited by them or altering them chemically. Then follows a discussion of the stoichiometry and kinetics of enzyme inhibition *in vitro*, including considerations of reversal of the inhibition and of the nature of the inhibited site. Aging of phosphorylated cholinesterase, resulting in irreversibility of the inhibition, is discussed in this chapter but without consideration of the altered electronic configuration of the enzyme inhibited by a monoalkylphosphoryl moiety, rather than by a dialkyl one, that renders protonation by an oxime difficult under physiological conditions. The third chapter in this section treats in greater detail the metabolism of phosphorus compounds *in vitro*, considering hydrolytic, oxidative and reductive reactions. The following chapter on inhibition of enzymes *in vivo* includes a discussion of the correlation between intravenous LD50's and I50's and ends with a section on

inhibition of enzymes in insects and other non-mammalian species. The two final chapters in this section consider metabolism of the organophosphorus compounds by mammals and insects and by plants, soil bacteria and soils themselves.

The section on Pharmacology in Mammals begins with an introductory chapter that presents the basic phenomena of cholinergic transmission, a few methods for studying the effects of chemicals on tissues and the usual effects of several common drugs. It is both surprising and disappointing that nothing is said here about methods for studying either the central or the peripheral mechanisms of pulmonary ventilation, which are of crucial importance in poisoning by the organophosphorus anticholinesterases. This is all the more surprising because some of the earliest work of Barnes' group, to which the author of the volume belongs, pertained to the actions of organophosphorus anticholinesterases on ventilatory activity.

The introductory chapter is followed in order by chapters on effects on organs *in vitro*, on organs *in vivo*, on mammals, on therapy for poisoning and on narcotic and demyelinating effects. These discussions are reasonable ones, in general; this reviewer can not agree with the statement, p. 323, that "P2-AM is usually found to be at least as effective therapeutically as atropine." In studies with rabbits, cats, dogs, monkeys and chimpanzees we find regularly that P2-AM alone raises the LD50 dose of such compounds as Sarin by only about 1.5-fold whereas atropine raises it by 2.5 to 3.0 times. A mixture of P2-AM and atropine raises the LD50 of Sarin by nearly 30 times. This reviewer can not agree either with Heath's statement that MINA and DAM are more effective against Sarin than P2-AM. For example, in experiments parallel to the last one summarized above a mixture of atropine and DAM raised the LD50 dose of Sarin by only about 4 times.

The final section, and chapter, of the book starts with a discussion of neuroeffector transmission in insects and then presents briefly the actions of organophosphorus anticholinesterases on important systems in insects. The general summation of this chapter, to the effect that no conclusion can be reached about the mechanism of lethality in insects of the organophosphorus cholinesterase inhibitors until more is known of normal nervous function in these animals, will serve perhaps to spur efforts by the small band of insectophilic physiologists to secure the basic information on which can be founded an understanding of the mechanism of death in poisoning of insects by organophosphorus compounds.

Although there are a few surprising lacks in this book (for example, there is no discussion of the types of cholinesterases in different tissues), on the whole the book seems to have achieved its purpose. It is a volume that will be of interest particularly to chemists and biochemists but will have distinct value as a summary of existing knowledge to practitioners of other scientific disciplines. It is rather interesting that suddenly the organophosphorus inhibitors of cholinesterase are the subjects not only of several review papers but also of the excellent book by O'Brien, of this book and of a forthcoming volume of Heffer's Handbuch. One wonders unavoidably about the forces shaping such a sudden outpouring of considerations of the same body of literature.

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