

Hespe, Nauta, Rekker, Timmerman, and deVries, presents the development of those classes of drugs which contain the benzhydryl moiety as a bioactive entity. A surprising number of drugs contain this moiety and represent several different classes of agents. Following a review of synthetic methods, the discussion centers on various "phases of manipulation". These include the classical approaches, by various synthetic substitutions, consideration of structural features, such as ether bond stability and base function, and correlation of ether bond stability and pK_a with linear free-energy parameters. Other physicochemical parameters are discussed in correlating structure and activity, including multiple regression analysis and influence of chirality. The roles of absorption, distribution, and biotransformation in relation to design are also considered, and this chapter is probably more closely related to the intent of the series than many of the others.

The remainder of the volume is taken up with reviews of a more conventional nature, but nonetheless highly informative, on the subjects of antiradiation agents, proteinase inhibitors, organ-imaging radiopharmaceuticals, x-ray contrast media, and formulation of agricultural pesticides. The chapter on the design of antiradiation agents, by Klayman and Copeland, presents a very good coverage of the more active compounds in each of the known classes of protective agents, with brief discussions of the nature of radiation damage, evaluation of potential agents, and theories of protection. This topic has not yet been treated successfully by correlation with physicochemical parameters, and in a review of this extent, none of the significant related aspects of radiation or thiol chemistry could be included.

The chapter on proteinase inhibitors by Okamoto and Hijikata covers quite adequately the development of agents with specificity toward proteinases with appropriate mention of the biological aspects involved. The same may be said of the chapters on organ-imaging radiopharmaceuticals, by Counsell and Ice, and x-ray contrast media, by Herms and Taenzer. Physical, chemical, and biological factors are considered in detail and make these chapters both highly informative and readable. The development of these agents, in the latter two chapters, is particularly well delineated and makes very interesting research stories.

The final chapter on agricultural pesticides, by Hartley, is concerned, of course, with the distribution, uptake, loss, and

toxicity of the pesticides in plants. The purpose of this chapter, in a series on drug design, is to perhaps encourage cross fertilization of ideas with mammalian medicinal chemistry. The discussions on physical and chemical methods of formulation of these agents show many similarities with the methods of drug formulations, with perhaps greater utilization of prodrugs. This chapter is certainly not inappropriate for this series on drug design.

In his review of Volume I, Burger wondered "what rabbit Ariens will pull out of an almost emptied hat" to fill future volumes. Some very interesting subjects were pulled out of the hat in this volume, but the nature of the subjects discussed has required a more conventional treatment than was perhaps envisioned at the outset. The information presented here should be of great value to those concerned with these topics and should be found in every library devoted to medicinal chemistry. Some of these topics have not been treated in similar fashion elsewhere.

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Biosynthesis. Volume 3. Specialist Periodical Reports. By T. A. Geissman, Senior Reporter. The Chemical Society, Burlington House, London. 1975. viii + 293 pp. 14 × 22 cm. \$11.00.

This volume, which reviews the literature of 1973, follows the format of previous volumes in the series. While it has been customary for authors to cite review articles which appeared in the year under consideration, a welcome innovation has been introduced in the chapter on biosynthesis of quinones in the form of brief summaries of earlier work so that the chapter can stand as a definitive modern treatment of the compound class. Chapters on terpenoids from C₅ to C₄₀, flavonoid polyphenols, alkaloids, and the physical methods used to study the biosynthesis of these compounds complete the volume.

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Corrections

1976, Volume 19

D. B. Rusterholz, C. F. Barfknecht, and J. A. Clemens: Ergoline Congeners as Potential Inhibitors of Prolactin Release. 2.

Page 101. In the final page makeup, some lines were misplaced in Results and Discussion, and the section in full should read as follows.

Results and Discussion

The results of the prolactin release inhibition assay are shown in Table I. The standard drugs ergocornine and apomorphine inhibited prolactin secretion by 60 and 29% at dosages of 10 μ g/rat and 1 mg/rat, respectively. The drug, "M-7" (14), which has been shown to be a potent dopamine agonist,²³ is found to have a strong inhibitory action in this assay, thereby adding further support to the contention that inhibition of prolactin release results from

dopaminergic agonism. The test compounds 4 and 6 have previously been shown to inhibit prolactin secretion in vitro when used in high concentrations.¹ In this assay 4 was relatively inactive, while 6 produced a 24% inhibition, which has only borderline significance at this dose level, but may exhibit a significant effect at higher doses. In the aminotetralin series 7-10, methoxy substituents on the aromatic ring did not produce active compounds. However, hydroxy substituents did appear to confer activity to the aminotetralin structure when the 2-amino group was tertiary. The dramatic increase in activity which occurs when going from the secondary amine 12 to the tertiary amine 13 emphasizes the importance of the tertiary amine to activity in these agents. The structural similarity between 13 and 14 strongly suggests that 13 is a dopaminergic agonist as well. We are now involved in the confirmation of dopaminergic activity in 13 and other compounds.