explain the difference between the UV and titration values.

pK_a of 4-(Benzylsulfonyl)-3*H*-1,2,3-triazole (3c). The mean apparent pK_a in water at 220 and 225 nm was 5.15. Potentiometric determination of apparent pK_a in 1:1 acetonitrile/water gave a value of 5.81 (MW = 223.250, neutralization equivalent = 225.464). Potentiometric titration in water was precluded by poor solubility.

Acknowledgment. We thank Matthew Teague for performing the pK_a measurements and Dr. Dan Pentek (Yale University Instrumentation Center) for the high-resolution FAB mass spectrometric measurements.

Note Added in Proof: Since this manuscript was submitted, the use of a tetrazole as an isostere for phosphonate has been described: Ornstein, P. L. European Patent 330,353, published August 30, 1989.

Registry No. **1a**, 15139-30-7; **1b**, 124603-61-8; **1c**, 27099-02-1; **2a**, 21239-87-2; **2b**, 29982-78-3; **2c**, 29982-79-4; **3a**, 79100-69-9; **3b**, 124603-62-9; **3c**, 79100-71-3; **4a**, 65479-47-2; **4b**, 124603-63-0; **4c**, 124603-64-1; **6a**, 124603-73-2; **6b**, 124603-74-3; **6c**, 124603-75-4; **7a**, 124603-76-5; **8a**, 124603-77-6; **9a**, 124603-78-7; **10a**, 124603-79-8; **11a**, 124603-80-1; AP-7, 85797-13-3; 2-mercaptoimidazole, 872-35-5; 4-mercapto-1,2,3-triazole, 75232-02-9; 3-mercapto-1,2,4-triazole, 3179-31-5; carbethoxy thiosemicarbazide, 65479-56-3; 2-hydroxythiophenol, 1121-24-0; ethyl 2-acetamido-7-bromo-2-carbethoxyheptanoate, 5183-26-6; ethyl 2-acetamido-6-bromo-2-carbethoxyhexanoate, 5183-27-7; ethyl 2-acetamido-5-bromo-2-carbethoxypentanoate, 52892-17-8; ethyl 2-acetamido-2-carbethoxy-7-[(2-hydroxyphenyl)thio]heptanoate, 124603-65-2; ethyl 2-acetamido-2-carbethoxy-6-[(2-hydroxyphenyl)thio]hexanoate, 124603-66-3; ethyl 2-acetamido-2-carbethoxy-5-[(2-hydroxyphenyl)thio]pentanate, 124603-67-4; ethyl 2-acetamido-2-carbethoxy-7-[(2-aminephenyl)thio]heptanoate, 124603-68-5; 2-aminothiophenol, 137-07-5; ethyl 2-acetamido-2-carboethoxy-7-[(2-hydroxyphenyl)sulfonyl]heptanoate, 124603-69-6; ethyl 2-acetamido-2-carbethoxy-7-[(2-hydroxyphenyl)sulfinyl]heptanoate, 124603-70-9; ethyl 2-acetamido-2-carbethoxy-5-[(2-hydroxyphenyl)sulfinyl]pentamate, 124603-71-0; ethyl 2-acetamido-2-carbethoxy-6-[(2-hydroxyphenyl)sulfinyl]hexanoate, 124603-72-1; methyl 2-amino-7-[(2-hydroxyphenyl)thio]heptanoate, 124603-81-2; methyl 2-amino-7-[(2-hydroxyphenyl)-sulfinyl]heptanoate, 124603-82-3.

Book Reviews

Advances in Biotechnology of Membrane Ion Transport. Edited by P. L. Jørgensen and R. Verna. Raven Press, New York. 1989. xv + 260 pp. 16.5 × 24 cm. ISBN 0-88167-423-0. $60.00.

This volume represents the proceedings of a Serono Symposia sponsored meeting of the same name that was held in L'Aquila, Italy on September 19–20, 1988. The purpose of the meeting was to bring together an international panel of experts on membrane transport processes to discuss timely biochemical, molecular biological, biophysical, and pharmacological aspects of this topic. Given the many significant advancements that have occurred in the field of ion transport over the last 5 years, this was a very ambitious undertaking. The proceedings of the meeting reflect the broadness of the organizers' approach. Unfortunately, this has resulted in a potpourri of minireview articles and minor scientific contributions that lack a high degree of cohesiveness.

The presentations in this book deal with ATPases (Na^+,K^+-ATPase, plasmalemmal Ca^{2+}-ATPase, sarcoplasmic reticulum Ca^{2+}-ATPase), ion channels (voltage sensitive Na^+, Ca^+, and K^+ channels, as well as the nicotinic acetylcholine receptor and neuronal Cl^- channels), and several membraneous processes that are tangentially related to ion transport (nucleocytoplasmic transport, viral fusion, and the structure of membranes). Lacking in this symposium were topics related to ion transport in bacteria and bacterial vesicle systems which have seen significant mechanistic advances over the last 5 years. Although there are a couple of reports which present biophysical studies, most deal with biochemical and molecular biological data.

Perhaps the topic best represented at this meeting was the Na^+ pump. The chapter by Lingrell et al. on cardiac glycoside sensitivity of the Na^+,K^+-ATPase is interesting and compliments nicely a report from Karlish's laboratory dealing with canrenone and endogenous ouabain-like substances. There is also a chapter by Jørgensen, a coorganizer of the meeting, on the structure and mechanism of the Na^+,K^+-ATPase from mammalian kidney. Current understanding of the structure of the plasmalemmal Ca^{2+}-ATPase, as determined by proteolytic digestion, is outlined by work from Carafoli's laboratory. Of the studies on ion channels that were reported, Catterall reviews data regarding the molecular properties of Na^+ and Ca^{2+} channels, while Lazdunski discusses the work from his laboratory on neuronal K^+ channels. Of interest to medicinal chemists is a chapter by Garay regarding the use of red blood cells to screen for selective inhibitors of transport systems. This listing is by no means complete, but cites some of the more notable contributions in this book.

As might be expected from a work which covers such a wide variety of areas, the review articles are timely, brief, and to the point, but cannot go into the depth that would interest a specialist in the field of ion transport. The original research reports are also of limited interest. Consequently, this book is directed to the nonspecialist, either someone with former knowledge of the field of ion transport who wants to be brought up to date or someone who wants to read a brief collection of reports to gain some appreciation of current trends in membrane transport.

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Safe and Effective Control of Acid Secretion. Edited by M. Mignon and J.-P. Galmiche. John Libby, London. 1988. xiii + 311 pp. 18 × 25 cm. ISBN 0-86196-176-5. $62.00.

This is a collection of presentations given at the International Symposium on Safe and Effective Control of Acid Secretion held in Fort-de-France/La Martinque, January 1988. The reader will find a broad range of topics from the physiology of gastric acid secretion to the socioeconomic aspects of ulcer disease management. The editors provided a balanced distribution of specific subjects within each topic. Readers who are unacquainted with this area of science will find this book an excellent and comprehensive learning tool, while those versed in the field will enjoy the in-depth and up-to-date nature of the chapters. The contributing authors include several internationally recognized investigators.

With the explosive interest in gastric acid secretion over the last 2 decades ignited by the introduction of the histamine H_2 receptor antagonist cimetidine, several questions needed to be addressed. Thus, the symposium was strategically designed to answer questions such as the following: what is our current understanding of the physiology and pharmacology of acid secretion, what are the safety issues with antisecretory therapy, what is thee pharmacological basis of treating reflux esophagitis with antisecretory drugs, and are there socioeconomic issues in the management of peptic ulcer disease.

The first four chapters of this book focus on the physiology of gastric acid secretion. Chapters on parietal cell biology, vagal regulation, neurohumoral regulation of gastrin and acid, as well as gastric mucosal trophicity are well done and current concepts in these important areas are expertly presented. The next four chapters deal with the pathophysiology and pharmacology of gastric acid secretion. Safety issues are the main topic of discussion in chapters 9–12. The following five chapters address the topic of duodenal ulcer disease. Reflux esophagitis and its management with gastric antisecretory agents, an interesting and at times controversial aspect of antisecretory therapy, are addressed in the next four chapters. Three excellent chapters consider the socioeconomic aspects of ulcer disease management. The symposium's final session is dedicated to a discussion of the problems and future of ranitidine therapy as they relate to treatment of esophageal reflux, prophylactic use in stress ulcers and maintenance therapy assessment by video endoscopy, and use in treatment of erosive duodenitis.

This book is well organized and provides the reader with a wide spectrum of information which successfully addresses the questions that have evolved since the introduction of antisecretory therapy and which are posed by the editors in the forward. Regardless of the depth of knowledge being pursued, the reader will find this book an interesting and informative experience.

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Serendipity. Accidental Discoveries in Science. By Royston M. Roberts. Wiley, New York. 1989. xviii + 270 pp. 15 × 23 cm. ISBN 0-471-60203-5. $12.95. Paper-bound.

The word serendipity was coined by Horace Walpole in 1754. On the basis of an ancient fable from Sri Lanka the term describes discoveries made by accident but with sagacity, i.e. by chance "favored by a prepared mind" (Pasteur). The history of drug discovery abounds with examples of serendipitous invention. In fact, only few "lead" compounds for new biological tests have been discovered strictly by planned researches. Most of them have turned up in systematic and often random screening programs or as a result of molecular modification of known metabolites. The fine-tuning in a series of candidate compounds for demanding clinical trials has almost always been based on molecular modification, even if this is directed by anticipated comparisons of chemical, steric, and physical characteristics (bioisosterism).

Professor Roberts has now given us the term pseudoserendipity to describe accidental discoveries in search for a defined goal, in contrast to true serendipity where something new is discovered by accident although it was not sought for.

The book is not restricted to medicinal chemistry although 21 out of 36 chapters belong in this field. Polymers, gravity, individual chemical elements, electromagnetism, organic reactions, fibers, explosives, plastics, archeological digs, radioactivity, gasoline additives, DNA, and crown compounds provide other examples for serendipitous achievements. This variety, from one end of science to another, makes for delightful and interesting reading. The whole history of physical and biological sciences unfolds in these pages in simple, understandable terms and style. Such easy reading should also encourage us to pinpoint our researches more critically so that, 100 years from now, serendipity may become a historical footnote.

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Nucleotide Analogues as Antiviral Agents. ACS Symposium Series 401. Edited by John C. Martin. American Chemical Society, Washington, D.C. 1989. viii + 190 pp. 15.5 × 23.5 cm. ISBN 0-8412-1659-2. $44.95.

This latest volume in the ACS Symposium Series consists of 12 chapters describing the synthesis, evaluation, and mechanism of action of nucleoside analogues as antiviral agents. The chapters are well written and present a logical and clear progression in the specific areas discussed. For example, chapter 1 presents a review of inhibitors of polymerases beginning with PAA and progressing to pyrophosphate analogues. Several of these chapters present an historical perspective and are very current with advances through 1988 reported. This book covers both chemistry and virology and consequently appeals to both disciplines. Chapter 2 for instance presents some interesting chemistry in the synthesis of acyclonucleoside phosphonates. Similarly, chapter 10, which deals with nucleosides and nucleotide analogues, is very nicely presented with a considerable amount of time spent on both chemistry and virology.

From a different perspective, chapter 3 deals with structure–substrate relationship of acyclonucleotide analogues from a biochemical point of view coupled with considerable discussion concerning molecular modeling. With use of MM2-modified free fields, three-dimensional energy maps for thymidine and ganciclovir were generated and the results were correlated with activity of some guanine analogues.

An excellent review of inhibitors of Herpes Simplex virus thymidine kinase is presented in chapter 7. This chapter describes the role of thymidine kinase in HSV infections, its mode of action and then proceeds to describe several series of compounds which are proven inhibitors of the enzyme.

Inhibitors of protein glycosylation are discussed in chapter 8, again beginning with a description of the role of this enzyme in herpes virus replication, followed by a discussion of the utility of this approach to HSV chemotherapy.

Chapters 11 and 12 are concerned with the inhibition of HIV. A series of nucleotide dimers which inhibit reverse transcriptase is discussed in chapter 11 and in vitro and in vivo results are presented. Finally, chapter 12 describes results obtained with oligonucleotides of 15–20 bases. The target here is the interference of genetic expression at the transcription or translation stage. This chapter begins with the design of oligonucleotide analogues and proceeds through cell uptake, binding, and in vitro evaluation against HIV.

In general, the chapters in this book are well written and organized and this volume is a good up to date account of progress in the nucleotide field.

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