rOH to give **33a** (200 mg, 11%): mp 140–141 °C; MS m/z 182 (CI^+, $[M + 1]^+$ of free base); ^1H NMR (D_2O) δ 1.62–1.71 (1 H, m, one of 5-CH_2), 1.97–2.08 (1 H, m, one of 5-CH_2), 3.34–3.60 (5 H, m, 4-CH, 6-CH_2, and 7-CH_2), 3.74 (1 H, ddd, J = 2.3, 6.0, and 12.2 Hz, endo-2-CH_2), 3.98 (1 H, dt, J = 3.0 and 12.2 Hz, exo-2-CH_2), 4.45–4.53 (1 H, m, 3-CH), and 8.75 (1 H, s, 3′-CH). Anal. ($C_8H_{11}N_3S$·$(COOH)_2$) C, H, N.

(b) *exo*-3-(1,2,4-Thiadiazol-5-yl)-1-azabicyclo[2.2.1]heptane Hydrogen Oxalate (34a). The mother liquor from the crystallization of **33a** above was treated with NaOMe (1 g, 18.5 mmol) for 2 h then evaporated. Water was added and extracted five times with CH_2Cl_2. The combined extracts were dried and evaporated to give a yellow oil which was treated with oxalic acid (350 mg, 3.8 mmol) in MeOH and evaporated. The residue was crystallized twice from MeOH/Et_2O to give **34a** (435 mg, 38%): mp 121.5 °C; MS m/z 182 (CI^+, $[M + 1]^+$ of free base); ^1H NMR (D_2O) δ 1.98–2.08 (1 H, m, one of 5-CH_2), 2.22–2.33 (1 H, m, one of 5-CH_2), 3.25–3.32, 3.34–3.44, and 3.50–3.60 (2 H, 1 H and 2 H, respectively, each m, 4-CH, 6-CH_2, and 7-CH_2), 3.82 (1 H, ddd, J = 2.0, 8.6, and 12.1 Hz, one of 2-CH_2), 3.89 (1 H, ddd, J = 2.8, 5.4, and 12.1 Hz, one of 2-CH_2), 4.02–4.10 (1 H, m, 3-CH), and 8.72 (1 H, s, 3′-CH). Anal. ($C_8H_{11}N_3S$·$(COOH)_2$) C, H, N.

The relative stereochemistry of compounds **34** were determined from a complete assignment of the COSY-45 NMR for **34b** in which additional crosspeaks were observed corresponding to ^4J coupling between transantiperiplanar protons as expected in a rigid bicyclic system of this type. These were found for H3/anti-H7, endo-H2/anti-H7, exo-H2/exo-H6, endo-H5/syn-H7, and endo-H6/syn-H7, conclusively proving the relative stereochemistry of these protons and thus that the thiadiazole moiety was exo (syn- and anti- for H7 refer to the disposition of these protons with respect to the bridge bearing the thiadiazole group). Similarly for **33b**, crosspeaks were observed for ^4J exo-H2/exo-H6 and ^4J endo-H2/anti-H7, thus defining the stereochemical relation of exo-H2 and endo-H2. Since ^3J exo-H2/H3 (11.5 Hz) > ^3J endo-H2/H3 (5.7 Hz), H3 was assigned as cis to exo-H2, making the thiadiazole substituent endo. This was confirmed by NOE experiments which demonstrated that H3 was on the same face of the molecule as exo-H2. These stereochemical assignments are consistent with the observed thermodynamic stabilities of the two isomers on base-catalyzed epimerization.

Molecular Modeling. 3,5-Dimethyl-1,2,4-oxadiazole and 3,5-dimethyl-1,2,4-thiadiazole were constructed with data from X-ray diffraction or microwave spectroscopy for the heterocyclic ring.[11] Ab initio molecular orbital calculations were carried out on these molecules with GAUSSIAN 80[9] at the STO-3G level. The wave functions obtained were used in DENPOT 80[8] to generate electrostatic potential maps using a 2-dimensional grid consisting of 900 calculation points (30 × 30) over the molecule and surrounding space, in the plane of the ring, from which the local minimum potentials adjacent to N2 and N4 were taken. Conformational analyses were carried out with the OPTIMOL program[21] within the Merck molecular modeling facility.[22] The energies of individual conformers were calculated at each 20° rotation around C3–C5′ after minimization with a molecular mechanics force field.[21] The *S* enantiomer was used in each case with the dihedral angle measured viewing down the C3–C5′ bond. Tables of these energies are available as supplementary material.

Acknowledgment. We thank our colleagues Dr. R. Herbert for NMR analysis, Dr. A. Richardson for technical assistance, and E. Brawn for typing this manuscript.

Supplementary Material Available: Microanalysis data for the compounds synthesized and conformational analysis energies for **33b**, **34b**, **38**, and **39** (3 pages). Ordering information is given on any current masthead page.

(21) Halgren, T., unpublished. OPTIMOL is based on MM2 (Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127) and differs mainly in the use of partial charges on atoms, instead of bond dipoles, and in the absence of unshared pairs on certain nitrogen and oxygen atoms.

(22) (a) Gund, P.; Andose, J. D.; Rhodes, J. B.; Smith, G. M. *Science* **1980**, *208*, 1425. (b) Smith, G. M.; Hangauer, D. G.; Andose, J. D.; Bush, B. L.; Fluder, E. M.; Gund, P.; McIntyre, E. F. *Drug Inf. J.* **1984**, *18*, 167.

Book Reviews

One and Two Dimensional NMR Spectroscopy. By Atta-ur-Rahman. Elsevier Science Publishers B. V., Amsterdam, The Netherlands. 1989. xx + 578 pp. 17 × 24.5 cm. ISBN 0-444-87316-3. $186.75.

In ever increasing numbers medicinal chemists are turning to advanced NMR experiments to solve complex structural problems. These problems vary from structure elucidation of natural products to probing the 3-dimensional structure of ligand–receptor complexes. To date, few texts are available for the medicinal chemist, as well as organic chemist, to expand his or her knowledge of NMR without getting bogged down in the mathematics of matrix algebra. This book provides, in my opinion, an excellent forum for the chemist who is familiar with the fundamentals of NMR to develop an understanding of the more sophisticated 1D and 2D experiments in common use today. This book clearly and concisely presents 1D and 2D experiments in terms of pulse sequences and simple vector models with clear concise illustrations.

The book is separated into 14 chapters of varying detail, each concentrating on a different type of NMR experiment. Chapter 1 provides a clear introduction into the general principles of NMR. Topics covered in this chapter include probe tuning, shimming, dynamic range problems, quadrature phase detection in both dimensions, coherence transfer, phase cycling, composite pulses, and rotation of vectors. Chapter 2 gives an excellent explanation of spin-echo and polarization transfer experiments. In this chapter the various modifications of the 1D INEPT and DEPT experiments are given. In order to aid the reader in developing an understanding of the applications of material present in the chapter, a short problem set (with answers) is included at the end of the chapter. These problems involve the structure elucidation of several natural products. Chapter 3 covers in limited detail the 1D INADEQUATE experiment for the determination of carbon-carbon connectivities. Chapter 4 presents a very good discussion of the theory of the nuclear Overhauser effect, presenting the various relaxation pathways. The 1D NOE difference experiment is presented and discussed in detail. Chapter 4 also includes a problem set at the end of the chapter. Chapter 5 gives a good nonmathematical introduction to the principles of 2D NMR. Chapters 6 and 7 cover the infrequently used, but historically important, techniques of heteronuclear and homonuclear J-resolved spectroscopy. Both chapters give examples of many different types of experiments and have problem sets at the end. Chapter 8 gives a very good (89 pages) discussion of homonuclear shift correlation spectroscopy. Topics covered in this very well-written chapter include coupling constants from phase-sensitive COSY spectra, peak shape, shaping functions, coherence transfer pathways in COSY spectra, COSY-45, phase-sensitive COSY, relay COSY, and SECSY spectra. Chemical shift correlations through cross-relaxation and exchange processes are covered in chapter 9. Chapter 9 presents a very good discussion of various NOESY experiments including heterorelayed NOESY and homorelayed NOESY spectra. Rotating-frame NOE or ROESY spectra and heteronuclear NOE or HOESY spectra are also discussed in this chapter. As with several other chapters, a problem set is included. Chapter 10 presents a discussion of

heteronuclear shift correlation experiments including inverse detection techniques. Chapter 11 presents a short (11 pages) introduction to cross-polarization in the rotating frame. In my opinion, the discussion of the HOHAHA experiment needs more detail and examples of its usefulness. Chapter 12 is an introduction to multiple-quantum spectroscopy. The 2D ^{13}C INADEQUATE experiment is discussed along with proton multiple-quantum spectroscopy and multiple-quantum filtered COSY spectroscopy. Chapter 13 is entitled Tackling the Structure. In this chapter the author does an excellent job of bringing together the information in the first twelve chapters to determine the structure of 7-hydroxyfrullanolide. Lastly, chapter 14 is one of the best introductions to the product operator approach to 2D-NMR spectroscopy that I have read. This chapter will be a valuable learning tool to prepare the reader to tackle the original research paper by Sorensen, Eich, Levitt, Bodenhausen, and Ernst, which is must reading for all who are serious about understanding 2D NMR.

In general the book is a very good text for the experienced scientist or advanced graduate student in medicinal or organic chemistry to expand his or her knowledge of NMR. The book contains references, though not exhaustive through 1987, with the references appearing at the end of each chapter. The NMR experiments are presented in terms of their pulse sequences with phase cycles included where possible. This is an excellent teaching and reference text, which has already found its way to our spectrometer console.

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Heterocyclic Compounds. Isoquinolines. Part Two. Edited by F. G. Kathawala, Gary M. Coppola, and Herbert F. Schuster. Wiley-Interscience, New York. 1990. xvi + 541 pp. 16 × 24 cm. ISBN 0-471-62856-5. $175.00.

This is the most recent volume of *The Chemistry of Heterocyclic Compounds* which has been published since 1950 under the initial editorship of Arnold Weissberger, and later, until Dr. Weissberger's death in 1984, under joint editorship with the present editor, Edward C. Taylor. Part one of the isoquinoline series was published in 1981. As a result of many factors, publication of part two has been long delayed and consequently the chapters differ from the ones projected in part one. The present volume is divided into four chapters describing halogenated and metallated isoquinolines, isoquinoline carboxylic acids, isoquinolines containing basic functions at the ring, and isoquinolines containing oxidized nitrogen functions. Related hydrogenated derivatives are also described in the four chapters. Each of the chapters is written by experts in the field. In every chapter is presented a detailed description of the synthesis, reactions, properties, structure, physical chemistry, and utility of practically every known compound in the specific class. A detailed list of references follows all chapters; however, despite recent updating, relatively few post-1980 citations appear. A subject index for the entire volume is also included.

The return on *The Chemistry of Heterocyclic Compounds* following its replacement by the discontinued parallel series entitled *General Heterocyclic Chemistry* will be welcomed as an old friend. The present editor plans to publish all forthcoming volumes in the general area of heterocyclic chemistry in this present series. Clearly, organic and medicinal chemists will welcome the return of this basic reference collection for information on heterocyclic compounds to their institutional libraries.

Staff

Biocompatibility—Interactions of Biological and Implantable Materials. Volume 1. Polymers. By Frederick Silver and Charles Doillon. VCH Publishers, Inc., New York. 1989. xiii + 306 pp. 16 × 24 cm. ISBN 0-895-73317-X. $45.00.

This book is divided into two major sections. Part I is a short course in biomaterials science, which includes chapters on (a) an overview of market size, tissue and implant components, the physical and mechanical properties of polymeric biomaterials, and a brief discussion of some recent books on the subject, (b) organ and tissue structure, (c) the tissue response to injury, (d) wound healing as it relates to implanted materials, (e) the chemistry and physics of polymers, (f) the analysis of such polymeric materials, and (g) the methods used to evaluate biocompatibility. Part II discusses the end-use applications of biomaterials and includes (a) would dressings and artificial skin, (b) replacement of skeletal soft tissue structures, (c) cardiovascular implants, (d) drug delivery biopolymers, and (e) metals, ceramics, and composite materials.

The discussions in this book begin with very fundamental concepts which assume almost no knowledge of the field on the part of the reader. A good deal of the text involves the normal organ systems and their interrelationships. For each of the methods discussed for evaluating a specific type of biocompatibility, quite complete compilations are given of the various methods which have been used. For many such type of biocompatibility, methods are given for in vivo, in vitro, and ex vivo analyses. It should be noted, however, there are few comparative evaluations given of the various methods described.

Although each chapter contains a bibliography, the book is not extensively referenced. A list of books covering various aspects of the discussions is included, however, which will help in locating specific discussions of interest. An index is provided.

This book will be particularly useful for neophytes to questions of polymer biocompatibility. The discussions of normal tissue and the response to injury are sufficiently detailed to serve as an introduction to anatomy, physiology, and the toxicology of implanted materials, and as such, the book will have a wide audience.

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Advances in Drug Research. Volume 18. Edited by Bernard Testa. Academic Press, New York, 1989. xiii + 549 pp. 15 × 23.5 cm. ISBN 0-12-013318-0. $60.00.

This is the latest in the excellent series edited by Dr. Testa. The basic philosophy underlying earlier voluimes is maintained: publication of a variety of reviews of broad general interest to the medicinal chemist and the pharmacologist, written by outstanding researchers in the fields. Consistent with his earlier volumes, Dr. Testa has written an amusing and thought-provoking preface, in this volume concerning writers of review articles.

In the opening chapter, Bernard Pullman presents a detailed exposition of Molecular Mechanisms of Specificity in DNA-Antitumor Drug Interactions, integrating aspects of chemical thermodynamics, quantum mechanics, stereochemistry and conformational analysis, and biology in a manner which makes for a most valuable reference work. A short chapter on The Structure and Receptor Binding of Steroid Hormones by William L. Duax and Jane F. Griffin is an update of the topic, and contains only a few literature citations prior to 1980. Similar comments apply to Aldose Reductase Inhibitors: Structure–Activity Relationships and Therapeutic Potential by Reinhard Sarges.

Opioid Receptors and Their Ligands: Recent Developments by Alan Casy is described by the author as a continuation of earlier reviews on central analgesics. Dr. Casy has again demonstrated his masterful ability to integrate organic chemistry and pharmacology in this important therapeutic area. I found the chapter on Purine Receptors and Their Pharmacological Roles by Trevor W. Stone to be the most readable and informative exposition of the topic that I have seen.

In Muscarinic Cholinergic Receptors and their Interactions with Drugs, M. Sokolovsky provides an update of progress in the field and brings some sense of order into the chaos of muscarinic agonism.

Consistent with previous volumes of the series edited by Dr. Testa, printing, proofreading, and documentation of the chapters is excellent. All of the chapters are well-written and the authors have cited large amounts of recent literature. Selection of the topics for the volume reflects contemporary interests in medicinal chemistry, and all chapters should have a broad appeal. The

volume is highly recommended.

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Cardiovascular Function of Peripheral Dopamine Receptors. Edited by J. Paul Hieble. Marcel Dekker, Inc. New York, 1990. xvii, 359 pp. 15.5 × 23.5 cm. ISBN 0-8247-8100-7. $125.00.

The 15th volume of this clinical pharmacology series brings together a wealth of information on peripheral dopamine receptors and their cardiovascular effects. The important differences between central and peripheral phenomena produced by a common neurohumor, dopamine, are emphasized. This volume deals with the consequences of activation of peripheral dopamine receptors impacting on the cardiovascular system, either the presynaptic inhibitory dopamine receptor, located on the adrenergic (DA_2 receptor), or the postsynaptic DA receptor, which mediates active dilation in certain highly vascular areas, including the renal and mesenteric beds. Evidence for a DA_1-like receptor modulating neurotransmission in sympathetic ganglia and for the actions of dopamine on adrenal dopamine receptors resulting in inhibition of adolsterone secretion is presented.

Dr. Hieble is joined by 29 contributors, all of whom have made significant contributions to the understanding of peripheral dopamine receptors. Significant are two chapters by the late Leon I. Goldberg and Jai Kohli, who played key roles in the development of dopamine pharmacology.

The book is divided into four parts. The first includes several introductory chapters describing receptor subclassification, model systems, and methods of assay. The second three chapters include discussions on the neuroinhibitory actions of dopamine agonists in vascular and cardiac tissue as well as effects on ganglionic neurotransmission. Part III, comprised of five chapters, deals primarily with the hemodynamic effects of dopamine receptor agonists in the intact animal, general descriptions of methods for analyzing dopamine receptor-mediated effects, and a description of the pharmacology of a new class of potent and selective dopamine-β-hydroxylase inhibitors. Part IV consists of four chapters on the effects of peripheral dopamine agonists in man. Included in this section is a chapter on the dopamine-mediated inhibition of aldosterone secretion emphasizing dopamine's endocrine effects. A subject index is included which is of great help in locating specific information.

This text will be of considerable interest not only to the dopamine receptorologists but also to cardiovascular clinicians and clinical pharmacologists. Medicinal chemists will find this a timely and current treatise on those agents which have been evaluated on peripheral dopamine receptors. Unfortunately, the stereochemistry has not been shown for all the structures presented.

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Pharmaceutical Chemicals in Perspective. By Bryan G. Reuben and Harold W. Wittcoff. John Wiley and Sons, New York. 1989. xviii + 518 pp. 16 × 24.5 cm. ISBN 0-471-84363-6. $69.95.

The 20th century has witnessed many revolutions but none as important and beneficial as the two-stage revolution in the medicinal treatment of diseases. First came the introduction of antiinfectious agents, which is still in full swing, especially in the antiviral fields, and second the approaches to the therapy of many functional, nutritional, degenerative, genetic, geriatric, and psychopharmacological disorders. We are now at the threshold of researches on orphan drugs for relatively rare diseases, for which a profitability motive will have to be considered, since it costs up to 150 million dollars to develop a novel chemical for clinicial use. The principal player in these efforts has been the pharmaceutical industry, especially its research-oriented chemical and experimental biology departments, and their coordination with clinical pharmacology units of research hospitals. The scientists of this industry are in the forefront of studies which have led to the healthier lives of many populations and to sharply increased longevity. They can be justifiably proud of their beneficial achievements.

The book by Reuben and Wittcoff provides a condensed survey of widely prescribed drugs, their chemistry, chemical syntheses—with tongue-in-cheek since the actual syntheses are not often divulged by the industrial chemists and engineers—their principal biochemical mechanisms of action, their drawbacks, their clinical utility, and their economic significance. These mainstays of the pharmaceutical industry are the out-in-front star performers but have to be backed up by the 1000 less widely used drugs one finds on the shelves of pharmacies. Then there are drugs on the drawing boards, studied on the basis of biochemical analogies, genetic engineering, and stereospecific syntheses which predict a picture of drug design over the next few decades. The present state of drug design has been overplayed; the H_2 histamine receptor antagonists were "designed" only to some extent. The medicinal chemists had to prepare and test 500 analogues before cimetidine with its apparently essential imidazole moiety could be chosen for clinical use; this requirement fell by the wayside when ranitidine, which does not contain an imidazole ring, began to rival cimetidine. Likewise, the QSAR calculations now routinely used in the industry to cut down on bioisosteric variants have not produced a breakthrough in searches for clinically useful agents. Neither have the hundreds of prostaglandin-derived structures led to specifically useful leukotriene drugs, inspite of excellent selective "leads".

For a student who wants to choose a career in the health sciences as well as for an administrator who wishes to increase researches in such a field, the chapters on the characteristics of the pharmaceutical industry and on patterns of illness and health care will be of great aid. They are followed by chapters on receptor theory, metabolite antagonists and agonists, and all-too-short sections on drug design and SAR which, if extended, would have illustrated the frustrating hurdles of medicinal chemistry. Then come the less profitable drugs, the "top-100" agents, and the orphan drugs. One of the authors is American, the other British, and together they offer the reader a balanced view of the multinational pharmaceutical industry. There are many fascinating background accounts that will make for interesting reading by chemists, biologists, and clinicians. The belated role of L-dopa in wakening *encephalitis lethargica* patients from a "sleep-conscious" horrible doom after *50* years caps these stories that everyone should read. There is a good subject index; references to review monographs and articles are adequate.

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Cell Activation and Signal Initiation: Receptor and Phospholipase Control of Inositol Phosphate, PAF, and Eicosanoid Production. Edited by Edward A. Dennis, Tony Hunter and Michael Berridge. Alan R. Liss, Inc., NY. 1989. xx + 387 pp. 18.5 × 26.5 cm. ISBN 0-8451-4705-6. $150.00.

This book is volume 106 of the UCLA Symposia on Molecular and Cellular Biology, New Series. It contains papers that were presented at the Lilly-UCLA Symposia conference on Cell Activation and Signal Initiation held in Keystone, Colorado on April 17–23, 1988 and includes an author index and an adequate subject index. Of the 39 papers, 33 were received for publication by the end of June, 1988 while the last six were received by September, 1988. This makes the bulk of the material almost two years old with most references to material before 1988. Twenty-four papers are reprinted from the *Journal of Cellular Biochemistry*, volumes 39 and 40, 1989. This represents two-thirds of the book's pages.

The table of contents divides the book into seven sections, the titles of which accurately describe the subjects of the papers they contain: (I) Cell Activation and Signal Initiation (a two page overview), (II) Phospholipase A_2 Mechanism, Cloning, and Inhibitors (six chapters), (III) Phospholipase A_2 Function, Activation, and Eicosanoid Production (nine chapters), (IV) Lipocortin Definition and Function (two chapters), (V) Phospholipase C and Cell Activation (three chapters), (VI) Protein Phosphorylation and Protein Kinase C (nine chapters), (VII) Inositol Phosphate

Metabolism and Ca^{2+} Mobilization (four chapters), and (VIII) PAF Formation and Function (five chapters). It would have been simpler for the reader if the chapters appeared in the book in the same order they appear in the table of contents, as opposed to the seemingly arbitrary order in which they are arranged (i.e., by the date received for publication).

The scope of the book is rather broad. Its chapters contain quite detailed information from different fields that would be of use to only a fraction of its readers. For example, in the chapter titled Design and Synthesis of Conformationally Restricted Phospholipids as Phospholipase A_2 Inhibitors, one finds several pages of experimental procedures, spectral data, and schemes relating to the synthesis of various inhibitor targets, while in the chapter titled Phospholipase A_2 Engineering: Design, Synthesis, and Expression of a Gene for Bovine (Pro)Phospholipase A_2, one can read in great detail just what the title implies, including the source of the plasmid and the exact strain of *Escherichia coli* used as its host. Since the chapters are in reality papers that were written in journal format, it is easy to identify those sections that are of interest (results and discussion) and those that might best be skipped if they are out of your field (materials and methods).

Medicinal chemists working in the fields of this book will probably not find it necessary to have copies on their desks. However, its additional chapters make it a book that should be found in the library, even those already subscribing to the *Journal of Cellular Biology*.

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Enzymes as Targets for Drug Design. Edited by Michael G. Palfreyman, Peter P. McCann, Walter Lovenberg, Joseph G. Temple, Jr., and Albert Sjoerdsma. Academic Press, San Diego, CA. 1989. xiii + 267 pp. 15.5 × 23 cm. ISBN 0-12-544030-8. $39.00.

The forum for this book was a symposium held on January 15–17, 1989 for and by scientists who had worked with Albert Sjoerdsma at The University of Chicago, at the National Institutes of Health, or at the Merrell Dow Research Institutes (Strasbourg and Cincinnati). The topics, therefore, are of limited scope; however, because of the broad interests and varied research carried out in the laboratories of Dr. Sjoerdsma throughout his highly productive career, this is not much of a drawback. The 18 contributed papers cover a variety of enzyme inhibition studies from the basic scientific aspects through to clinical results. In the first chapter J. R. Crout states that "...it is one thing for a compound to inhibit an enzyme and quite another for that compound to become a marketed pharmaceutical product." That seems to be the theme of this book, to show both the basic science and clinicial applications, but to indicate that just because the in vitro (and in vivo) results are promising, it does not mean that the company should break ground for a new research facility.

For those interested in historical events leading to the discovery of a drug or fascinated by the early results that were used as a basis for a drug-design approach, this will be a worthwhile addition to your personal library. Many of these early studies involve the contributions of Sjoerdsma.

In addition to a brief overview of marketed drugs that inhibit different enzymes and a nice summary of the mechanism-based enzyme inhibitors (including transition-state analogues) that were developed at Merrell Dow since Sjoerdsma joined the company, the following enzyme systems are discussed (note that some of the chapters deal with proteins and receptors rather than enzymes): phosphatidylinositol glycosyl membrane proteins, ADP-ribose polymerase, dopamine receptors (including dopa decarboxylase and dopamine β-hydroxylase), β-adrenergic receptors, steroid 5α-reductase, hydroxylases (aromatase, dopamine β-hydroxylase, and aromatic amino acid hydroxylases), aromatic amino acid decarboxylase, monoamine oxidase, enzymes in polyamine biosynthesis (ornithine decarboxylase, *S*-adenosylmethionine decarboxylase, aminopropyltransferase, arginine decarboxylase, and spermidine synthase), γ-aminobutyric acid aminotransferase, intra blood–brain-barrier IgG synthesis in HIV, proteases, and enzymes in eicosanoid biosynthesis (cyclooxygenase, thromboxane synthase).

Other nice features of the book are that each chapter has a summary of the results described in that chapter and the index is comprehensive with considerable cross referencing. For followers of the work of Albert Sjoerdsma and his colleagues or for those interested in selected enzymes for drug design this is a must addition to your library.

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Hypertension–Pathophysiology, Diagnosis, and Hypertension–Pathophysiology, Diagnosis, and Management. Vol 1 and 2. Edited by John H. Laragh and Barry M. Brenner. Raven, New York, 1990. xxxviii + 2360 pp. 22 × 29 cm. ISBN 0-88167-493-1. $325.00.

Hypertension is a multifaceted disease often associated with an increased risk of other cardiovascular complications such as coronary heart disease and stroke. This relatively asymptomatic disease is also often associated with a number of metabolic complications such as glucose intolerance, hyperlipidemia, hyperinsulinemia. These multiauthored volumes do a superb job in describing the disease, its complications, and available as well as potential future treatments.

These volumes contain seven sections and 250 chapters. The chapters vary in length from 9 to 30 pages. The sections are divided into background and historical aspects, epidemiological dimension of hypertension, diet and hypertension, circulatory and target organ pathophysiology of hypertensive disease, blood pressure regulation in normal and hypertensive states, clinicial and laboratory evaluation of hypertensive disorders, and pathophysiology, diagnosis, and treatment of specific forms of hypertension.

The chapters are well-written and contain up-to-date references as well as relevant older as well as historical references. The chapters often contain both experimental as well as clinical findings. There are few, if any, important aspects of hypertension that are not covered in this book. Of special interest are chapters dealing with the genetic basis of hypertension and recent epidemiological findings in this disease. The chapter dealing with the genetic susceptibility of hypertension discusses the relative importance of environmental vs genetic factors in the familial development of hypertension. Additionally, the relationship between inherited lipid disorders, obesity, and hypertension are adequately covered. Several chapters deal with the trends in the prevalence of hypertension and the effects of treatment on morbidity and mortality. Results of recent large-scale clinical trials utilizing different treatment regimens are described in a number of chapters. An interesting chapter discusses the epidemiology of hypertension among the elderly.

Mentioned in a number of chapters are the relationships between diet and blood pressure. The often complex relationships between blood pressure and magnesium and calcium intake, vegetarian diets, fat intake, protein intake, and alcohol intake are discussed in individual chapters. These are areas often overlooked in other texts on hypertension and are a welcome addition to this text.

The chapter on the clinical development of antihypertensive drugs was an excellent, current description of the difficulties and potential pitfalls involved in the development of new antihypertensive agents. The last two chapters describe the renin inhibitors and orally active angiotensin II antagonists as examples of potential new therapeutic agents on the horizon. Other areas, e.g. potassium channel openers, adenosine receptor agonists, serotonin agonists and antagonists, etc., were not mentioned in this section.

Overall this book should serve as an excellent compendium to those involved in both the treatment and understanding of hypertension. The rationale and theory behind relevant concepts are adequately discussed and assist in making this text easy to understand and follow.

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