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BOOK REVIEWS

Organic Reactions, Volume 72. Editor-in-Chief: Scott A. Denmark (University of Illinois at Urbana-Champaign). John Wiley & Sons, Inc.: Hoboken, NJ. 2008. x + 690 pp. $140. ISBN 978-0-470-42374-5.

This volume of *Organic Reactions* consists of two chapters: "Electrophilic Amination of Carbanions, Enolates, and Their Surrogates" by Ciganek and "Desulfonylation Reactions" by Alonso and Nájera. The book concludes with a cumulative list of chapter titles by volume, an author index of Volumes 1−72, and a chapter and topic index of Volumes 1−72.

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Nuclear Receptors as Drug Targets. Methods and Principles in Medicinal Chemistry, Volume 39. Edited by Eckhard Ottow and Hilmar Weinmann (Bayer Schering Pharma AG, Berlin, Germany). Series edited by R. Mannhold, H. Kubinyi, and G. Folkers. Wiley-VCH Verlag GmbH & Co. KgaA: Weinheim. 2008. xxiv + 498 pp. $215. ISBN 978-3-527-31872-8.

It is a safe bet that nearly everyone reading this review has used a nuclear receptor-modulating drug. From over-the-counter cortisol for topical inflammation, to the daily prescription rosiglitazone for type II diabetes, to tamoxifen, the most widely used cancer drug in the world, nuclear receptor-targeted compounds are highly successful and treat a range of banal to acute conditions. Indeed, nuclear receptors have been anecdotally referred to as "nature's drug targets" because of their unique functional niche. They are predominantly nonmembrane-associated, intracellular receptors that rapidly mediate changes in gene expression in response to largely lipophilic small molecules capable of dissolving directly into the cell. We are fortunate to have effectively harnessed for therapeutic purposes this class of transcription factors, which evolved to allow distant tissues to respond to small molecules secreted from various regions of a complex organism.

In this fine new volume edited by Ottow and Weinmann, the nuclear receptor superfamily is examined as targets for drug discovery and development in both great detail and for an audience of chemists. This book achieves impressive depth without sacrificing the breadth necessary to cover the 48 established human receptors. Two introductory chapters, including one by the editors, provide a concise but comprehensive overview of functional paradigms of nuclear receptors, as well as the history of this class of proteins as drug targets. In addition, these chapters begin to introduce methods that are commonly used to study nuclear receptors and that may be unfamiliar to some chemists; the presentation of experimental methodology continues through the remaining chapters in this volume as well.

Eleven detailed chapters covering the established drug target members of the nuclear receptor superfamily follow these introductory sections. These include three on the estrogen receptor, two on the progesterone receptor, one each on the androgen, glucocorticoid, vitamin D, peroxisome proliferator-activated, and retinoid-X receptors, and a chapter focused on a single condition, cardiovascular disease, that can be attacked via several of the targets listed above, plus the mineralocorticoid, retinoic acid, and liver-X receptors. Two chapters then address emerging nuclear receptor targets, including those of the relatively less characterized NR4A family, as well as the drug- and xenobiotic-detecting receptors: pregnane-X and constitutive androstane. Finally, a chapter covering the use of chemical libraries for the discovery of receptor modulators completes the volume. Throughout, success stories related to the generation of selective agonists and antagonists of receptor function are presented and are folded into discussions of the associated structural and organismal biology required to achieve desired therapeutic goals. At the same time, the authors cover the medicinal chemistry of lead identification and development in impressive detail, making this volume useful to biologists and clinicians as well as to synthetic chemists.

This is an excellent book for scientists interested in adding or expanding expertise in nuclear receptor drug discovery to their skill set. The chapters are timely, well referenced into the 2008 literature, and focused on the chemistry of successful and emerging therapeutic small molecules. In light of the trajectory of this field of study, it is probably a safe bet that the future will see a range of improved as well as completely novel nuclear receptor-modulating drugs added to those already enhancing human health.

Matthew R. Redinbo, Ph.D.* and Yuan Cheng,
University of North Carolina at Chapel Hill

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