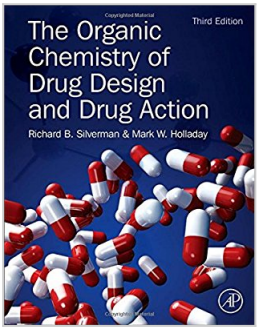

The Organic Chemistry of Drug Design and Drug Action, Third Edition

By Richard B. Silverman Ph.D Organic Chemistry, Mark W. Holladay

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The Organic Chemistry of Drug Design and Drug Action, Third Edition, represents a unique approach to medicinal chemistry based on physical organic chemical principles and reaction mechanisms that rationalize drug action, which allows reader to extrapolate those core principles and mechanisms to many related classes of drug molecules.

This new edition includes updates to all chapters, including new examples and references. It reflects significant changes in the process of drug design over the last decade and preserves the successful approach of the previous editions while including significant changes in format and coverage.

This text is designed for undergraduate and graduate students in chemistry studying medicinal chemistry or pharmaceutical chemistry; research chemists and biochemists working in pharmaceutical and biotechnology industries.

- Updates to all chapters, including new examples and references
- Chapter 1 (Introduction): Completely rewritten and expanded as an overview of topics discussed in detail throughout the book
- Chapter 2 (Lead Discovery and Lead Modification): Sections on sources of compounds for screening including library collections, virtual screening, and computational methods, as well as hit-to-lead and scaffold hopping; expanded sections on sources of lead compounds, fragment-based lead discovery, and molecular graphics; and deemphasized solid-phase synthesis and combinatorial chemistry
- Chapter 3 (Receptors): Drug-receptor interactions, cation-π and halogen bonding; atropisomers; case history of the insomnia drug suvorexant
- Chapter 4 (Enzymes): Expanded sections on enzyme catalysis in drug discovery and enzyme synthesis
- Chapter 5 (Enzyme Inhibition and Inactivation): New case histories:
  - for competitive inhibition, the epidermal growth factor receptor tyrosine kinase inhibitor, erlotinib and Abelson kinase inhibitor, imatinib
  - for transition state analogue inhibition, the purine nucleoside phosphorylase inhibitors, forodesine and DADMe-ImmH, as well as the mechanism of the

multisubstrate analog inhibitor isoniazid
    - for slow, tight-binding inhibition, the dipeptidyl peptidase-4 inhibitor, saxagliptin
- Chapter 7 (Drug Resistance and Drug Synergism): This new chapter includes topics taken from two chapters in the previous edition, with many new examples
- Chapter 8 (Drug Metabolism): Discussions of toxicophores and reactive metabolites
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Editorial Review

Review
"This book is a tour de force in the title area....This book adopts a novel format that focuses on the rational chemical underpinnings to both drug discovery and drug development. It seeks to illuminate the workings of drugs at the molecular level. Thus, this book contrasts with the traditional presentation which is organized around various classes of drugs....This book would be appropriate for advanced undergraduate students and graduate students and would probably be well suited as a text for course applications, especially at the graduate level. It is strongly recommended to scientists who are seeking an efficient introduction to medicinal chemistry, background in a specific drug principle or category, or a dose of inspiration."--Bruce E. Maryanoff, R.W. Jouhnson Pharnaceutical Research Institute, JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, Vo. 115, No.12, 1993 "For the first time the principles of medicinal chemistry/pharmacology are collected in a unified, well-organized and clearly presented fashion. It is so clearly written that it will be of value to both students and veteran scientists...My congratulations to Dr. Silverman in consolidating such a multiplicity of facts and data so as to truly begin to reduce medicinal chemistry from a hybrid of chemistry, pharmacology and related sciences to a single, clearly defined, rationalized discipline."--CARL KAISER, Ph.D., Director, Medicinal Chemistry, NOVA PHARMACEUTICAL CORPORATION "The author shows an uncanny ability to present the salient principles in a systematic, well-balanced and logical way...The book will turn out to be very popular with students because the material is presented clearly...The numerous superbillustrations included are used very effectively by the author to communicate and/or clarify concepts and ideas."--William C. Groutas, Ph.D., Professor of Chemistry, WICHITA STATE UNIVERSITY "I find [Chapter 8] to be an unusually comprehensive, clear and well organized discussion on prodrugs. Although the concepts are complex, they are presented in a logical, easily understood format. Dr. Silverman's use of schematics to illustrate both chemical and biochemical principles is especially effective and should be easily comprehended by the intended audience. I found myself reading for interest and enjoyment rather than searching for mistakes. The references are focused and current. It should become a standard text in short order."--Anthony A. Sinkula, Ph.D., THE UPJOHN COMPANY "I was favorably impressed with the clarity of Dr. Silverman's writing style which made the material interesting and easy to read...Treatment of the material is quite comprehensive without being overly detailed and the referencing and illustrations are well chosen and at about the right level."--John G. Topliss, Ph.D., PARKE-DAVIS "This book emphasizes the organic chemical aspects of medicinal chemistry....The organization of this book and the clarity of presentation are outstanding....The book very clearly presents medicinal chemistry as a unified discipline based on sound principles of organic chemistry. It is highly recommended to medicinal chemists as well as to all others entering into the field or concerned with the science of medicinal chemistry." --Journal of Medicinal Chemistry

From the Back Cover

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About the Author

Professor Richard B. Silverman received his B.S. degree in chemistry from The Pennsylvania State University in 1968 and his Ph.D. degree in organic chemistry from Harvard University in 1974 (with time off for a two-year military obligation from 1969-1971). After two years as a NIH postdoctoral fellow in the laboratory of the late Professor Robert Abeles in the Graduate Department of Biochemistry at Brandeis University, he joined the chemistry faculty at Northwestern University. In 1986, he became Professor of Chemistry and Professor of Biochemistry, Molecular Biology, and Cell Biology. In 2001, he became the Charles Deering McCormick Professor of Teaching Excellence for three years, and since 2004 he has been the John Evans Professor of Chemistry. His research can be summarized as investigations of the molecular mechanisms of action, rational design, and syntheses of potential medicinal agents acting on enzymes and receptors.

His awards include DuPont Young Faculty Fellow (1976), Alfred P. Sloan Research Fellow (1981-1985), NIH Research Career Development Award (1982-1987), Fellow of the American Institute of Chemists (1985), Fellow of the American Association for the Advancement of Science (1990), Arthur C. Cope Senior Scholar Award of the American Chemical Society (2003), Alumni Fellow Award from Pennsylvania State University (2008), Medicinal Chemistry Hall of Fame of the American Chemical Society (2009), the Perkin Medal from the Society of Chemical Industry (2009), the Hall of Fame of Central High School of Philadelphia (2011), the E.B. Hershberg Award for Important Discoveries in Medicinally Active Substances from the American Chemical Society (2011), Fellow of the American Chemical Society (2011), Sato Memorial International Award of the Pharmaceutical Society of Japan (2012), Roland T. Lakey Award of Wayne State University (2013), BMS-Edward E. Smissman Award of the American Chemical Society (2013), the Centenary Prize of the Royal Society of Chemistry (2013), and the Excellence in Medicinal Chemistry Prize of the Israel Chemical Society (2014).

Professor Silverman has published over 320 research and review articles, holds 49 domestic and foreign patents, and has written four books (The Organic Chemistry of Drug Design and Drug Action is translated

into German and Chinese). He is the inventor of LyricaTM, a drug marketed by Pfizer for epilepsy, neuropathic pain, fibromyalgia, and spinal cord injury pain; currently, he has another CNS drug in clinical trials.

Dr. Mark W. Holladay is Vice President of Drug Discovery and Medicinal Chemistry at Ambit Biosciences (San Diego, California) where he leads drug discovery programs in oncology and autoimmune diseases and has contributed to compounds in clinical development. He began his drug hunting career at Abbott Laboratories where he achieved the position of Volwiler Associate Research Fellow as a medicinal chemist and project leader in the Neurosciences Research Area. He also conducted collaborative drug discovery research as a member of contract research organizations including Biofocus and Discovery Partners International. He is a co-author on over 70 peer-reviewed research articles, reviews, or chapters and is named as an inventor on over 40 patents and patent applications. Dr. Holladay earned his undergraduate degree from Vanderbilt University, his Ph.D. at Northwestern University under the direction of Professor Richard B. Silverman, and conducted postdoctoral studies with Professor Daniel H. Rich at the University of Wisconsin-Madison.

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