

## Book Reviews

**Structure-based Ligand Design. Vol. 6.** Edited by Klaus Gubernator and Hand-Joachim Bohm. Wiley: Weinheim. 1998. 147 pp. \$135.00. ISBN 3-527-29343-4.

The pharmaceutical drugs that have been derived by structure-based ligand design are relatively few. However, this method of drug discovery should become ever more successful with the rapidly increasing number of protein structures being solved. Volume 6 of "Methods and Principles in Medicinal Chemistry" presents a collection of success stories in structure-based drug design. Chapters 1 and 2, written by the editors, give a very good overview of the basic principles. Chapter 3, written by E. A. Lunney and C. Humblet, discusses the development of renin inhibitors and the way results from these studies enhanced the development of HIV-1 protease inhibitors. The remainder of the book is a series of up-to-date reviews from various contributors discussing the development of inhibitors for metazincins, beta-lactamase, sialidase, and HIV protease. Chapter 8, written by H.-J. Bohm, is the only chapter that details the computational approaches used in structure-based ligand design. This volume concludes with a chapter summarizing the prospects of structure-based ligand design. The editors succeed in their attempt to "present a series of real-life stories from practitioners in the field".

Volume 6 of this series would be a good basic introduction into the field of structure-based ligand design for investigators new to the field. It provides insights into the trials and tribulations others in the field have gone through to obtain useful inhibitors. However, this volume lacks the details necessary to provide the reader with the knowledge of how one would actually perform structure-based design of new inhibitors. Many of the computational approaches used, such as AUTODOCK and GRID, are only mentioned. Additionally, for a field as visual as structure-based ligand design, I found the figures were very small, making it difficult to glean any information from them. This reviewer found the book well written and well edited, but it would probably only be useful to students or medicinal chemists interested in any of the individual reviews.

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**ZEKE Spectroscopy.** By E. W. Schlag (Technische Universität München). Cambridge University Press: Cambridge and New York. 1998. x + 277 pp. \$64.95. ISBN 0-521-58128-1.

All atoms and molecules exhibit quasi-hydrogenic electronic states, known as Rydberg states, which consist of an optical electron bound to a positively charged, many-electron core via a potential that is asymptotically Coulombic. Rydberg states are grouped energetically into series converging on ionization limits corresponding to particular core states. Near an ionization limit, the density of Rydberg states in a given series is proportional to  $n^3$  (where  $n$  is the "effective" quantum number), and Rydberg states are therefore densely packed near threshold.

In a field-free Rydberg state,  $l$  and  $m_l$  are good quantum numbers for the optical electron. In the presence of external fields, this symmetry can be broken, and  $l$ -mixing and  $m_l$ -mixing can occur. Near an ionization threshold, where the density of states is large,  $l$ -mixing and  $m_l$ -mixing can result from stray electric fields of the order of 40 meV/cm. In a high- $n$  Rydberg state that has been optically prepared to possess a small  $l$  value, stray electric fields induce  $l$ -mixing, leading to high- $l$  components that are essentially decoupled from the core electrons. In the presence of stray ions, long-range interactions lead to  $m_l$ -mixing, resulting in states having lifetimes of the order of 80–100  $\mu$ s, which is 2 orders of magnitude greater than the lifetime predicted for  $n > 100$  Rydberg states in the absence of mixing.

Since these long-lived  $l, m_l$ -mixed states exist near threshold, the optical electron has near-zero kinetic energy, thus prompting the terminology *zero kinetic energy* (ZEKE) states. The present book provides a review of the experimental techniques involved in the study of ZEKE states, as well as a literature survey of results currently available in ZEKE spectroscopy. Professor E. W. Schlag is ideally suited to provide a review of this field, since he and his co-workers have pioneered in the development of this new spectroscopic technique.

Dr. Schlag's monograph is the text of an extended set of invited lectures that he gave at Cambridge University while a Fellow of Sidney-Sussex College. The style is informal and sometimes even chatty, as befits the format of the original presentation. Schlag begins with a brief historical presentation of spectroscopy in general before concentrating on the techniques of photoionization spectroscopy, photoelectron spectroscopy, and resonantly enhanced multiphoton ionization spectroscopy including mass analysis. Schlag goes on then to introduce a direct forerunner of ZEKE spectroscopy, namely threshold spectroscopy, which involves the detection of zero kinetic energy electrons by making use of the zero angular divergence of these electrons even after extraction by a small draw-out field. Following this historical review, the basic elements of ZEKE spectroscopy are introduced from an experimental perspective. In the generic variant of this technique, a molecular beam is intercepted by a laser that can be tuned (resonantly) over an ionization threshold. One to two microseconds following the laser pulse, a pulsed electric field is applied across the ionization region, thus extracting the ZEKE states which formed during the time delay (which also served to permit the directly produced electrons and ions to disappear). The electrons resulting from this field ionization of the ZEKE states are then allowed to transit a drift tube and are detected by a multichannel plate. Alternatively, cations produced from field ionization of the ZEKE states can be mass analyzed in a time-of-flight mass spectrometer. What results is a high-resolution (limited by the resolution of the laser employed) spectrum of the threshold region that is comparable to the photoelectron spectrum for the first ionization event, but which continues to higher energies, exhibiting a distinct feature for each cationic state encountered. In principle, then, the basic ZEKE spectrum is the first derivative of the photoionization spectrum (but at 3 orders of magnitude greater resolution), with the detection of the ZEKE states serving to filter out the continuum ionization that underlies (and degrades) the photoionization spectrum.

Schlag goes on to describe methods for enhancing the resolution of the basic ZEKE technique, including ramping the extraction pulse and "slicing" the extraction pulse, and then proceeds to a survey of current results. Along the way, one is introduced to high-resolution ZEKE spectroscopy of benzene (and substituted benzenes), molecular clusters, and metal clusters, to free-radical spectra, to ZEKE spectroscopy of anions (involving the photodetachment threshold and, presumably, dipole bound states as the ZEKE precursors), and to ZEKE investigations of hydrogen bonding.

The book is divided into two parts: *Basics* and *Mechanisms and applications*. Part I serves as a general introduction to ZEKE spectroscopy and, in fact, reads like a long abstract for Part II. There are over 300 references (more than one-third of these are since 1994, and more than two-thirds since 1990) and an Appendix that lists high-precision ionization potentials obtained with ZEKE spectroscopy.

This is an enjoyable book, both in terms of style and content. It conveys the excitement inherent to a new area of research and provides suggestions for future directions (including applications of synchrotron radiation at third-generation sources). I recommend this book as one to read quickly to gain an orientation to this important field, and then to re-read and savor at leisure.

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