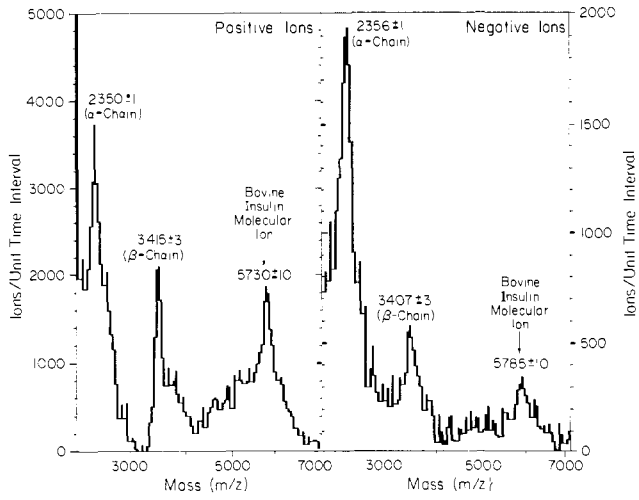


**Figure 1.** $^{127}$I-PDMS spectra of bovine insulin recorded over a 1.5-h period with a 90-MeV $^{127}$I (+20) beam current of 2000 $s^{-1}$.

a PDP-15 computer operating as a multichannel analyzer. Mass calibrations were made by using $(Cs_2I)^+$ cluster ions in the positive ion spectrum and $(CsI_2)^-$ cluster ions in the negative ion spectrum.

The experiment was performed so that the mass spectrum from each scan was added to the previous scans at the rate of 2000 scans $s^{-1}$. The "growing" mass spectrum was monitored on a graphics terminal linked to the computer. We first set the acceleration voltage for positive ion analysis and commenced the $^{127}$I beam irradiation. Only a few moments of data collection were needed before it became apparent that the insulin molecular ion was indeed present in the mass spectrum as well as lower mass ions in the region of the $\alpha$- and $\beta$-chain molecular weights. The polarity of the acceleration voltage was then reversed, and a search was made for negative ions of insulin. The mass spectrum was weaker but a mass pattern similar to that for the positive ions was observed. Careful measurements of the positive and negative ion spectra were made for a 1.5-h period involving $10^7$ separate mass scans (or $10^7$ incident I ions). A smooth exponentially decaying background (characteristic of ion-induced desorption using TOF) was subtracted from the gross spectra, and masses for the prominent peaks were calculated from the positions of the centroids of the mass peaks in the insulin spectrum and the cesium iodide cluster calibration ions. These results are summarized in Figure 1, which shows the positive and negative ion spectra in the mass region $m/z$ 2000–7000. Several mass peaks were observed below $m/z$ 2000 but these were not analyzed in this experiment. In addition, there was evidence for a peak at $m/z \sim 12000$, which presumably is a dimer ion of insulin.

The ion in the vicinity of the molecular weight of insulin has $m/z$ 5730 ± 10 and a yield of $3 \times 10^{-4}$ per incident $^{127}$I. The isotopically averaged molecular weight (C = 12.011) of bovine insulin is 5733. Thus, this molecular ion appears to contain all the pieces of the highly complex structure of insulin. The lower mass ions are at $m/z$ 3415 ± 3 and 2350 ± 1. The molecular weights of the $\alpha$ and $\beta$ chain of bovine insulin are 3398 and 2335, respectively. There is little doubt that the fragment ions are associated with these two pieces of insulin, but it is clear that something else is attached to them—perhaps a water molecule. The negative ion spectrum shows additional evidence for small molecule or ion attachment: the highest mass ion is at $m/z$ 5785 ± 10 and the apparent $\alpha$ and $\beta$ chain related negative fragment ions are at $m/z$ 3407 ± 3 and 2356 ± 1. This has been the first opportunity to examine gas-phase ion formation of such a complex species large enough to adopt a well-developed tertiary structure. Association of small neutral molecules or counterions into the complex structure may be important for the formation of a singly charged gas-phase ion, particularly when there are so many charge centers in the molecule.

An important milestone in mass spectrometry development has been realized with the detection of gas-phase molecular ions of insulin. This is not only because it is an important molecule for biomedical applications but also because it is near that semantic boundary in mass space beyond which a peptide becomes a protein.

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**Registry No.** Bovine insulin, 11070-73-8.

# *Book Reviews*

**Nuclear Chemical Engineering.** By M. Benedict (Massachusetts Institute of Technology), T. H. Pigford (University of California, Berkeley), and H. W. Levi (Hahn-Meitner-Institut für Kernforschung, Berlin). McGraw-Hill Book Company, New York. 1981. xv + 1008 pp. $37.95.

The first edition of this book was published in 1957 and has been widely recognized as the reference work on chemical engineering practice in the nuclear industry. Some 24 years later, and after a long period in preparation, the second edition is finally available. Although the general outline and style generally conform to those of the original book, this second edition may be regarded as an entirely new book: the amount of material presented has approximately doubled and a third author, Hans Levi, now shares the credit with Manson Benedict and Thomas Pigford.

Chapters 1–3 set the stage for the remainder of the book and introduce the concepts required to fully appreciate the substance of the developments presented in Chapters 4–14. It is to be noted that Chapter 3 contains a particularly helpful introduction to the area of nuclear fuel management, a topic generally poorly covered in the literature.

Solvent extraction, uranium, thorium, zirconium, and hafnium are covered in Chapters 4–7 while the processing and properties of irradiated fuel, actinide elements, and other reactor materials are dealt with in Chapters 8–10 as well as in a disappointing new chapter entitled Radioactive Waste Management (Chapter 11). Isotopic separation principles and processes are discussed in Chapters 12–14.

The large amount of new material is a reflection of the vast changes which have occurred over a period of nearly 25 years and a result of a somewhat greater emphasis on process description. The main asset of the book remains the same however: the authors' extraordinary ability to combine scientific and engineering principles in an area to which they have given an identity and contributed extensively—nuclear chemical engineering.

Albert J. Machiels, *University of Illinois*

**Synthetic Aspects of Biologically Active Cyclic Peptides—Gramicidins and Tyrocidines.** By N. Izumiya, T. Kato, H. Aoyagi, M. Waki, and M. Kondo. Halsted Press (Wiley), New York. 1979. xii + 166 pp. $29.95.

The purification, characterization, synthesis, and study of biologically active peptides isolated from microorganisms have long been areas of intensive scientific investigation. Of particular interest have been those peptides which possess antibiotic activities. Because they contain uncommon and D-amino acids and are usually cyclic, peptide antibiotics have presented unusual challenges to structural and synthetic peptide chemists. These properties have however made them very valuable as models for the development of methods for the chemical synthesis of cyclic peptides and for biosynthetic and conformational studies. Over 300 different peptide antibiotics have been discovered to-date. Of these,

perhaps none have been studied more thoroughly and provided more valuable information than the gramicidins and the tyrocidins, which are the main topic of this timely book written by experts in the field.

After a brief historical introduction in Chapter 1, the isolation and characterization of the 30-membered cyclic decapeptide gramicidin S, the tyrocidines, linear gramicidins, gramicin J, and the cyclic dodecapeptide antibiotic gratisin are presented in Chapter 2. The body and quintessence of this monograph are contained in the succeeding three chapters. These focus on the synthesis by solution and solid-phase methods, structure–activity studies, and conformational studies by X-ray, ORD, CD, NMR, IR, and EPR techniques of gramicidin S, the tyrocidines, and their analogues. These chapters provide a wealth of information and make for fascinating reading. Chapters 6 and 7 are interesting and lucid accounts of studies on how these peptides work and how they are biosynthesized. The final chapter deals with the isolation, characterization, synthesis, and structure–activity relationship studies of a different but also intriguing class of cyclic peptides—the phytotoxic AM-toxins.

This is a well-written authoritative monograph on multifaceted and interesting peptides. This book, a noteworthy first on the gramicidins and the tyrocidins, has much to recommend it to peptide chemists, peptide biophysicists, and peptide biologists.

**Maurice Manning,** *Medical College of Ohio at Toledo*

**Metal Ions in Biological Systems. Volume 11. Metal Complexes as Anticancer Agents.** Edited by Helmut Sigel (University of Basel). Marcel Dekker, Inc., New York. 1980. xx + 425 pp. $55.00.

The eight review chapters in this volume are written primarily by chemists interested in the synthesis and chemistry of metal antitumor agents. The first chapter contains an overview of the history and scope of metals evaluated as antitumor agents. Subsequent chapters deal specifically with Pt, Ru, and Cu complexes, with metal complexes containing alkylating agents, and with metals binding to antitumor antibiotics. The final chapter describes studies on the interaction of anticancer drugs with enzymes. The chemical, biochemical, and clinical aspects of the Pt antitumor agents are treated in most detail and this reflects the utility of the compounds. In general, the volume contains a balanced view of the field and can be recommended to chemists interested in metallodrugs.

**Luigi G. Marzilli,** *Emory University*

**Annual Review of Physical Chemistry. 1981. Volume 32.** Edited by B. S. Rabinovitch, J. M. Schurr, and H. L. Strauss. Annual Reviews, Palo Alto. ix + 478 pp. $20.00.

This is the Hildebrand centennial volume of "Annual Reviews of Physical Chemistry". Unlike some other books of this sort, the editors of this work were faced with the pleasant prospect that the object of the centennial was alive, well, and able to contribute an extremely interesting chapter on the history of solution theory, beginning with the author's graduate study under van't Hoff and Nernst and emphasizing the author's experimental work on non-ionic solutions and its implications.

The remaining 15 chapters are all interesting and well written. Following the initial emphasis on liquids, one finds the following topics: D. W. Oxtoby on vibrational relaxation, H. L. Friedman on electrolyte solutions, S. C. Greer and M. R. Moldover on critical phenomena, B. J. Alder and E. L. Pollock on polar fluids, and C. Williams and co-workers on polymer collapse. The section by M. B. Weissman on fluctuation spectroscopy avoids light scattering and, among other innovations, treats an experiment which relies operationally on ensemble rather than time averaging. Other topics covered include the study of exotic molecules in extreme vacuum—by radio astronomy, gas–surface interactions, and electron correlations in molecular systems.

**George D. J. Phillies,** *The University of Michigan*

**Physical Chemical Properties of Drugs. Medicinal Research Series. Volume 10.** Edited by Samuel H. Yalkowsky, Anthony A. Sinkula, and Shri C. Valvani. Marcel Dekker, Inc., New York. 1980. XVII + 384 pp. $45.00.

Volume 10 of "Medicinal Research Series" contains ten chapters covering the question of the relationship of physicochemical properties and drug activity. Topics such as the prediction of $pK_a$ values, quantitative relationships between $pK_a$, ionization, and drug potency are covered in the first two chapters. Limitations and the role of the Hansch partition coefficient are discussed in Chapters 3 and 4.

Computation of partition coefficients from molecular structures by a fragment addition method is discussed in Chapter 5. Other chapters include topics such as solubility and partitioning in drug design, thermodynamic considerations in physical property improvement through prodrugs, simultaneous determination of the solubility parameters, molecular connectivity, and molecular surface area, volumes, and their use in structure–activity relationships. The calculation of water solubility of organic compounds from a knowledge of their octanol–water partition coefficients and melting points, discussed in Chapter 6, represents an interesting approach in drug evaluation.

The variety of topics covered in this book covers a good part of the theoretical and practical means to estimating and understanding the pharmacologically relevant physiochemical properties of drug molecules. The book should be of great value for drug evaluation and theoretical studies in structure–activity correlations and for those who are involved in testing of new drugs.

The time has arrived for agencies involved in massive evaluation of new drugs to use computer techniques to calculate important parameters for biological activity. An approach is offered in this book. This book will be a valuable reference for pharmacologists, biochemists, and chemists involved in research and drug evaluation.

**Mohamed E. Nasr,** *Starks C.P., Inc.*

**Phase Diagrams. A Literature Source Book.** By J. Wisniak (BenGurion University of The Negev). Elsevier Scientific Publishing Co., Amsterdam and New York. 1981. x + 2102 pp. $319.50 (two-part set).

These books are the tenth title to appear in the "Physical Sciences Data Series" of Elsevier. The goal of the compiler of these volumes has been to make it possible for a scientist or engineer to determine easily whether the phase diagram for a particular binary or multicomponent, organic or inorganic mixture has been published and, if so, to locate it. This is accomplished with an alphabetic listing by elements present in published phase diagrams with citations to the 17 381 relevant publications which have appeared between 1900 and 1980. Each citation includes a *Chemical Abstracts* number, which should prove useful in the case of difficult-to-obtain books and periodicals.

These source books are the well-organized product of a computerized search. As such, they contain no text other than a preface and a half-page guide to the tables, no phase diagrams, and no evaluation of the literature cited. Each prospective purchaser will have to decide whether it is more cost effective to do his own computerized literature searches or purchase these very expensive volumes.

**Stanley I. Sandler,** *University of Delaware*

**Stochastic Nonlinear Systems.** Edited by L. Arnold (Universität Bremen) and R. Lefever (Université Libre de Bruxelles). Springer-Verlag, Berlin. 1981. viii + 237 pp. $29.50.

This book contains the invited papers of the workshop on Stochastic Nonlinear Systems in Physics, Chemistry and Biology held at the University of Bielefeld, West Germany, October 5–11, 1980. Twenty-two papers are included covering a variety of topics of relevance to mathematicians, physicists, chemists, and biologists interested in stochastic phenomena. The main topics include: the transition from deterministic to stochastic behavior, the approximation of stochastic processes, the description of internal fluctuations, long-term behavior of stochastic systems, external fluctuations and noise-induced transitions, stochastic behavior in model systems, space–time processes, phase transitions, irreversible thermodynamics, Markov processes, and time reversibility. Of primary interest to chemists are several excellent papers pertaining to chemical instabilities, the kinetics of phase separation, and stochastic bistable systems.

**George C. Schatz,** *Northwestern University*

**New Synthetic Methodology and Biologically Active Substances.** Edited by Z-I. Yoshida (Koyoto University, Japan). Elsevier, Amsterdam and New York. 1981. x + 282 pp. $78.00.

The sixth in a series entitled "Studies in Organic Chemistry", this volume contains a collection of plenary and invited lectures from the First International Kyoto Conference on New Aspects of Organic Chemistry (December 4–7, 1980). "New Synthetic Methodology and Biologically Active Substances" was selected as the first topic in a series of triannually scheduled conferences to address new developments in organic chemistry. The specific topics discussed include polyene cyclizations in steroidal systems (W. S. Johnson), organoaluminum-mediated syntheses (H. Nozaki), asymmetric syntheses utilizing chiral heterocyclic ligands (T. Mukaiyama), asymmetric syntheses utilizing chiral phosphine–transition metal complexes (M. Kumada et al.), selectivity in organic synthesis as influenced by palladium (B. M. Trost), 1-oxacephems (W. Nagata), steroid hormones (T. Kametani), pheromones (K. Mori), asymmetric reactions applied to *d*-α-tocopherol (G. Saucy et al.), approaches to biologically active heterocycles (Y. Ban et al.), cycloadditions in industrial syntheses (H. Konig), chemical studies of bioactive microbial secondary metabolites (H. Umezawa), synthesis of formylmethionine transfer RNA from *E. coli* (M. Ikehara et al.), and novel peptide ionophores (V. T. Ivanov). An average of 33 references is given for each of the fourteen lectures.

**John A. Soderquist,** *University of San Francisco*