Additions and Corrections

Migration of an Excess Proton upon Asymmetric Hydration: $H^+[(CH_3)_2O](H_2O)_n$ as a Model System [*J. Am. Chem. Soc.* **1999**, *121*, 4443−4450]. HAI-CHOU CHANG, JYH-CHIANG JIANG, INA HAHNDORF, SHENG H. LIN, YUAN T. LEE, AND HUAN-CHENG CHANG*

Page 4443, column 2, line 15: 225 kcal/mol should be 226.8 kcal/mol, 3 kcal/mol should be 4.6 kcal/mol, and pyridine should be dimethylamine. Line 18: pK_b of 9.80 versus 5.25 of pyridine should be pK_b of 4.20 versus 3.32 of dimethylamine.

Page 4450, column 2, line 34: pK_b = 8.92 should be pK_b = 4.20.

JA995524H

10.1021/ja995524h
Published on Web 08/31/1999

Book Reviews

Electrochemistry. By Carl H. Hamann (Universitat Oldenburg, Germany), Andrew Hamnett (University of Newcastle, United Kingdom), and Wolf Vielstich (Universitat der Bundes-wehr Munchen, Germany). Wiley-VCH: New York. 1998. xvii + 423 pp. $61.95. ISBN 3-527-29096-6.

This book provides an introduction to the field of electrochemistry with an emphasis on fundamentals and industrial applications. The target audience is students and researchers within the physical sciences and engineering fields. According to the authors, the intent of this book is "to provide a wide coverage of electrochemistry and, in conjunction with suitable lectures, provide students with a working knowledge of the principles of electrochemistry that could serve as a foundation for independent study". I believe the authors have achieved their objectives. The book contains a detailed table of contents, 10 chapters, and an index. References included span the time period from the mid-1970s to the mid-1990s, with a large number of references given to other textbooks in related fields. The references are not exhaustive by any means. The authors have elected not to give problems at the end of each chapter.

The heart of this book lies in Chapters 2−5. Chapter 2 focuses on the concepts and theory of electrolyte conductivity and ionic mobility and their relation to equilibria and transport processes in solution. This is a well-written, self-contained chapter that contains important details about the nature of electrolytes in solution. Included in this 50+-page chapter are details about the measurement of conductivity and transport numbers, dependence on concentration, and relationship to equilibria processes such as the determination of the ionic product of water, dissociation constants, and solubility product constants.

Chapters 3 and 4 are the traditional chapters found in most standard electrochemistry textbooks on electrode potential, electron transfer kinetics, and mass transport. These two chapters alone encompass ca. 150 pages of text. Chapter 3 describes the thermodynamics of electrode potentials and their measurement, liquid junction and membrane potentials, the double-layer structure at phase boundaries including metal and semiconductor electrodes, and describes reference electrodes and the electrochemical series. The application of potential difference measurements to the determination of dissociation constants, solubility product constants, and pH can be found in this chapter as well. Overall, this is a nice, informative chapter. Chapter 4 contains too much and probably should have been divided into several smaller chapters. It is in Chapter 4 that one is introduced, albeit very briefly in many cases, to the Bulter−Volmer equation, theoretical treatments of electron transfer, rotating disk voltammetry, microelectrodes, adsorption processes, metal deposition and dissolution, underpotential deposition, corrosion, photoelectrochemisty, etc. From this electrochemist's perspective, it would have been nicer to have seen more on theoretical treatments of electron transfer, ultramicroelectrodes, and adsorption processes.

Chapter 5 is the "techniques/methods" chapter that provides a discussion of cyclic voltammetry (CV), ac measurements, and spectroelectrochemistry. The CV section contains a nice discussion of electrode surface films, with representative CVs given of platinum and/or gold in KOH or H_2SO_4 solutions. The spectroelectrochemistry section is rather limited in breadth in that it only includes information about infrared spectroelectrochemistry, electron spin resonance, and electrochemical mass spectroscopy and a few brief details on microbalance methods, STM, and optical methods (ellipsometry). Chapter 6 provides further information on reaction mechanisms, with details given on hydrogen and oxygen electrode reactions as well as some information on electro-organic reactions.

The remainder of the textbook (Chapters 7−10) is dedicated to "aspects of applied electrochemistry", with a particular focus on industrial applications. Specific topics covered include ionically conducting salts and melts as electrolytes (Chapter 7), industrial electrochemical processes such as electrolysis, electrochemical extraction, electrocatalysis, electrosynthesis (Chapter 8), batteries, fuel cells, and electric vehicles (Chapter 9), and "analytical" applications/methods including chemical sensors, ion-selective electrodes, and polarography (Chapter 10). The battery/fuel cell chapter is the most comprehensive of all these chapters. The other chapters, particularly the "analytical" chapter, are less detailed. For example, little information, if any, is given about electroanalytical methods and applications such as thin-layer electrochemistry, bulk electrolysis, chemically modified electrodes, ultramicroelectrodes (bands, arrays), and square wave voltammetry.

Overall, this is a solid book in physical electrochemistry, which could serve as a good resource for graduate courses in this area or to the industrial/academic chemist who wants to learn more about the underlying principles of pure and applied (industrial) electrochemistry.

Maryanne M. Collinson, *Kansas State University*

JA985686Y

10.1021/ja985686y

Integration of Pharmaceutical Discovery and Development: Case Histories. Volume 11. Pharmaceutical Biotechnology. Edited by Ronald T. Borchardt, Roger M. Freidinger, Tomi K. Sawyer, and Philip L. Smith. Plenum Press: New York. 1998. xxix + 607 pp. $125.00. ISBN 0-306-45743-1.

This text is the 11th in a biotechnology series that has focused on the delivery, stability, formulation analysis, metabolism, and pharma-

cokinetics of protein therapeutic agents. Although some of the case histories in this volume describe the discovery and development of peptide drugs, this book has the broader objective of illustrating the advantages of integrating development issues such as metabolism and bioavailability into the discovery and development process of all drugs as early as possible. To prove this point, 24 case histories from more than 10 pharmaceutical companies (with contributions from academic investigators in one case) are described by the original investigators. These examples include discussions of the objectives and strategies, chronological progression of events with respect to breakthroughs and dead ends, and ultimately the successes or failures of the searches for a wide variety of novel therapeutic agents. Specific examples include investigations of HIV protease inhibitors, reverse transcriptase inhibitors, angiotensin II antagonists, renin inhibitors, thrombin inhibitors, LHRH agonists and antagonists, somatostatin agonists, endothelin receptor antagonists, antiherpesvirus agents, ester prodrugs of β-lactam antibiotics, hematoregulators, inhibitors of 5α-reductase, α_{1A} receptor antagonists, inhibitors of secretory phospholipase A_2, CCK-B receptor antagonists, CCK-A agonists, growth hormone secretagogues, carbonic anhydrase inhibitors, and melanotropic peptides.

A valuable aspect of these case histories is that they contain detailed information describing compounds that failed to become drugs, and how these problems were overcome using alternate approaches. Although extremely significant to the cost of new drug discovery and development, such negative results are usually given little attention in the literature. The message from most of these examples is that metabolism and bioavailability issues were often major obstacles to the development of the compounds described. Therefore, the overall theme of this book is that development issues should be integrated as early as possible into the discovery process, since too much time, human effort, and money may be wasted on pursuing compounds that fail in animal and human testing because of metabolism and bioavailability limitations.

Because the time from the initial synthesis of a drug candidate to its approval as a new drug is typically 10−15 years and since the preclinical period alone is usually 3−5 years, each case history in this text describes the efforts of many investigators over at least 3 and sometimes as many as 15 years. Consequently, most of the studies were begun in the 1980s. Since pharmaceutical companies are not quick to publish their results, the most recent references in this book date from 1996. However, the timeliness of the case histories is often enhanced by the inclusion of previously unpublished results. The overall value of these studies is that each represents a review of the discovery and development of a class of new therapeutic agents by a particular group of industrial investigators during the last 10−20 years. A reader interested in the history of the pharmaceutical industry or the process of drug discovery would find this book significant in that it describes in great detail pharmaceutical drug discovery and development strategies immediately prior to the widespread introduction of combinatorial chemistry.

Many of the case histories in this book illustrate the inherent weaknesses and inefficiencies of existing strategies that failed to incorporate drug metabolism and bioavailability early in the drug discovery process. For example, in the pursuit of renin inhibitors at Abbott Laboratories, 1400 drug candidates were synthesized and evaluated using traditional methods over 3.5 years until a potent novel renin inhibitor was discovered. Then, this lead compound was found to lack oral bioavailability due to hepatic first-pass metabolism and poor intestinal absorption. Returning to the beginning of the discovery process, additional compounds were synthesized and evaluated until the peptide-based renin inhibitor zankiren was identified out of 4000 candidates and found to show meaningful oral absorption and bioavailability. In contrast, the case history of the discovery and development of cyclic HIV protease inhibitors at DuPont Merck included from the outset assays for metabolism, formation of toxic metabolites, and genotoxicity. In addition, Caco-2 intestinal epithelial cell assays were used to predict drug absorption in order to prioritize lead compounds. Only after the drug passed these tests did animal experiments begin in preparation for phase I clinical trials. The lesson to be learned from these case histories is that years of human effort and much money may be saved by screening for essential drug characteristics such as metabolism and absorption in addition to pharmacological potency toward a specific receptor during the drug discovery phase.

The trend toward early integration of drug metabolism, pharmacokinetics, and bioavailability within the drug discovery process is continuing as pharmaceutical investigators realize the extra costs of leaving these essential drug studies until late in drug development. Furthermore, these important changes are being accelerated as industrial drug discovery groups are reorganized around combinatorial synthetic methods and high-throughput screening assays. It is interesting to note in these case studies that few pharmaceutical companies are incorporating toxicity studies within the discovery process. Until this oversight is corrected, the majority of lead compounds will fail due to toxicity during animal and human testing, with great cost in terms of human effort and resources.

Richard B. van Breemen, *University of Illinois College of Pharmacy*

JA985750B

10.1021/ja985750b

Handbook of Surface and Colloid Chemistry. Edited by K. S. Birdi. CRC Press: Boca Raton, FL. 1998. $139.95. 738 pp. ISBN 0-8493-9459-7.

The stated purpose of this handbook is to cover the most recent developments of both the theoretical and experimental aspects of systems related to surfaces and colloids. With so many recent innovative applications and characterization techniques in surface science, this certainly cannot be an exhaustive treatment.

The book does an excellent job in reviewing the fundamental principles of colloid chemistry. The physical properties and behavior of surfactants, micelles, foams, emulsions, polymers, and thin films are adequately reviewed. There is a full chapter devoted to the physics of lipids and proteins at bio-interfaces, with a good description of the action of lung surfactants.

Several characterization techniques are reviewed as separate chapters. Dielectric spectroscopy is used as a method of monitoring how emulsions destabilize. Light scattering is used to track aggregation processes in colloidal systems, with a particular emphasis on fractal aggregates. The final chapter covers scanning tunneling microscopy and atomic force microscopy techniques, certainly falling within the scope of providing some of the most recent characterization techniques of colloid chemistry.

The applications highlighted cover vastly different areas. Two chapters describe the use of colloidal systems for the preparation of novel materials using templating strategies. The first approach uses micellar systems to control both the size and the shape of metal and semiconductor nanoparticles. The second approach uses lipid monolayers to control nanoparticle growth. Drug-loaded nanoparticles are reviewed as a biomedical application. Finally, the use of surfactants in oil recovery is described.

Overall, this is an excellent resource for fundamental principles and for a sampling of recent applications in colloid science. It is definitely a book any colloid chemist would want to keep handy, and it is an interesting read for scientists in other fields wanting to get an appreciation of colloid chemistry. However, the reader should be aware that this is not an exhaustive review. For example, the recent interest in the electronic properties of colloidal metals and semiconductors is not thoroughly reviewed. Also, this book is not meant as a source for preparative techniques.

Jean-Claude Bradley, *Drexel University*

JA995686D

10.1021/ja995686d