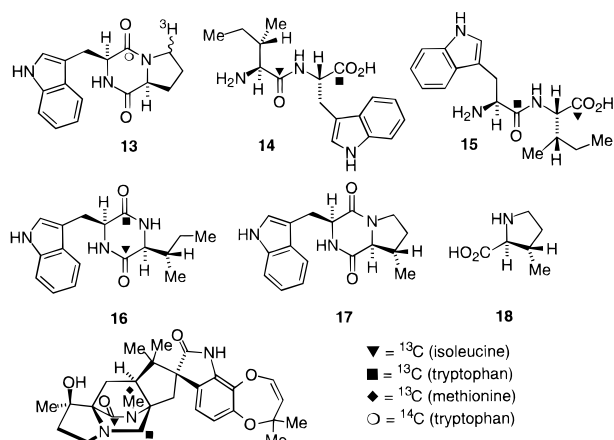


Additions and Corrections

Studies on the Biosynthesis of Paraherquamide A. Origin of the β -Methylproline Ring [*J. Am. Chem. Soc.* **1996**, 118, 7008–7009]. EMILY M. STOCKING, JUAN F. SANZ-CERVERA, ROBERT M. WILLIAMS,* AND CLIFFORD J. UNKEFER

The correct stereochemistry for compounds (**16**) *cyclo*-L-tryptophan-L-isoleucine, (**17**) *cyclo*-L-tryptophan-L- β -methylproline, and (**18**) L- β -methylproline in Figure 1 is shown below. The authors are indebted to Dr. Jeremy Everett for bringing this error to our attention.



JA9754158

Electron Transfer from C_{76} (C_{2v}) and C_{78} (D_2) to Radical Cations of Various Arenes: Evidence for the Marcus Inverted Region [*J. Am. Chem. Soc.* **1997**, 119, 5744–5745]. DIRK M. GULDI* AND KLAUS-DIETER ASMUS

The correct notation for the C_{76} and C_{78} isomers throughout the paper should be C_{76} (D_2) and C_{78} (C_{2v}).

JA975412V

Facile Metathetical Exchange between Carbon Dioxide and the Divalent Group 14 Bisamides $M[N(SiMe_3)_2]_2$ ($M = Ge$ and Sn) [*J. Am. Chem. Soc.* **1996**, 118, 10912–10913]. LAWRENCE R. SITA,* JASON R. BABCOCK, AND RIMO XI

After publication, we have become aware of prior work by Wannagat and co-workers in which they describe a related metathetical exchange process that occurs between carbon dioxide and $NaN(SiMe_3)_2$ to produce, along with 1,3-bis-(trimethylsilyl)carbodiimide (85% yield), a mixture of products arising from secondary reactions [Wannagat, U.; Kuckertz, H.; Krüger, C.; Pump, J. *Z. Anorg. Allg. Chem.* **1964**, 333, 54–60]. We regret this omission, however, it does not affect the findings or conclusions of the present work in which the synthetic utility of this form of heterocumulene metathesis is demonstrated for subvalent Group 14 compounds.

JA975414F

Chemical Structure of Blepharismine, the Photosensor Pigment for *Blepharisma japonicum* [*J. Am. Chem. Soc.* **1997**, 119, 5762–5763]. GIOVANNI CHECCUCCI, RICHARD K. SHOEMAKER, ELISABETTA BINI, RONALD CERNY, NENGBING TAO, JAE-SEOK HYON, DOMENICO GIOFFRE, FRANCESCO GHETTI, FRANCESCO LENCI, AND PILL-SOON SONG*

Page 5762: Richard Shoemaker's initial appeared incorrectly as S. in the journal.

Page 5762: The ring system of the structure shown in Figure 1 should be named benzodiazanthrone, instead of naphthodiazanthrone. The ring system linked by the bond 8-8' is dihedrally twisted, and the lack of a CD signal may be attributable to a racemic mixture of the two possible enantiomers. We thank Prof. Heinz Falk for pointing out the correct naming and asymmetry of the blepharismine structure.

JA975413N

Computer Software Reviews

Axum Version 5.0 for Windows. MathSoft, Inc.: 101 Main Street, Cambridge, Massachusetts, 02142; (617) 577-1017. \$199.95.

Axum 5.0 is a technical graphics and data analysis program. This version comes on eleven 3.5 in. 1.4 megabyte disks and is compatible with the DOS/Windows 3.x, Windows NT, and Windows '95 operating systems. MathSoft recommends a minimum 486-computer with 16 megabytes of memory and 14–20 megabytes of disk space depending on the installation procedure chosen. A math co-processor is also recommended but is not required. Hence, Axum is a reasonable choice for high-end academic research or industrial computers but will be more demanding of older, microlab academic computers.

Unlike many available software packages that also render technical graphics and perform data analysis, Axum is geared toward scientific applications rather than business applications. This is reflected throughout the program, including the ability to change the precision of the data with a single click on an icon and the inclusion of many mathematical functions, scientifically-important graph options, and a programming language to perform sophisticated data analysis. An important weakness of the program is the lack of an easy procedure within the program to insert complex characters into labels or titles (for example, Greek characters or mathematical symbols), although the

availability of tool bar buttons for fast addition of superscripts and subscripts to text is an improvement over previous versions of Axum. Additional features of the program include the ability to cut and paste comments, equations, and other figures (such as a chemical model) from any Windows-compatible word processor or graphics program into an Axum graph, in addition to the expected ability to cut and paste graphs generated with Axum into word processor programs.

In general, Axum is icon-driven and most commands are easily executed by using a tool bar that is similar to those used in most word processors and other graphics programs written for Windows and Macintosh platforms. As in older versions of Axum, the keyboard can be used to execute most commands by using combinations of the ALT, CTRL, and SHIFT keys. This is cumbersome, however, and the program works much more smoothly with the mouse.

Data can be imported in the usual ASCII format or can be imported directly from several popular spreadsheets like Excel, Quattro Pro, Paradox, and Lotus. Data can also be deleted or copied to new data sheets or new locations within the same data sheet by dragging or cutting and pasting individual data cells or entire data columns.

To make a graph, the user must click on the icon specifying a two-dimensional plot or a three-dimensional plot. This causes a menu of

self-explanatory icons to appear that allows the user to pick the style of plot needed. For example, in the two-dimensional case the user might pick a line, scatter, line plus scatter, bar, pie, or other type of graph. Furthermore, users in the chemical profession will appreciate the variety of three-dimensional graphs that are possible including slices, contours, projections, and three-dimensional surfaces. To generate the graph, the user highlights the data in the input file to be plotted (the user may select whole columns of data or just individual cells) and then clicks on the desired plot-type icon. This procedure can be shortened by adding frequently-used plot-type icons to the main tool bar.

It is simple to add a graph to an existing graph or change the data in an existing graph by using the drag and drop option or icons and tool bar commands to overwrite old data. It is also possible to make a graph by using data from multiple data sheets, and this is made considerably easier by the program's ability to have multiple windows open at the same time, such as several data windows and the graph window. This feature is also helpful if the user is manipulating the data and wants to observe the effect of these changes on the graph.

Graphs can be formatted several different ways. For example, they can be single panel or multipanel, can have a box around them or not, can be scaled and resized, or any of several other options too numerous to list. In addition, it is possible to combine two graphs on a single page, either side by side or overlaid on top of each other. A significant improvement over Axum 4.0 is the new ability to insert an axis break, or skip a range of values in a given axis.

The data are not saved with the graph which is significantly different from many other technical graphics programs and may cause problems if the user is used to saving everything once. A problem encountered with previous versions of the program is that sometimes a saved graph file will have difficulty linking to the appropriate saved data file, resulting in a blank graph and error messages. However, it is possible to save sets of graphs, data, and programs together under one "project"

heading. Graphs can be exported to common standard formats such as TIFF and BMP, but no postscript version is available.

Another important feature of Axum is its ability to do a wide variety of data analysis. This includes descriptive statistics (e.g., mean, sum, standard deviation, and finding the minimum and maximum values) correlation matrix, frequency distribution, and analysis of variance. The results are placed in new columns in the data sheet without altering the original data. The program also allows the user to perform linear and nonlinear regression and curve fitting (polynomial, log, power, etc.) and operate on the data using addition, subtraction, multiplication, log, exponential, and trigonometric functions. The results of these manipulations can be used to create new graphs such as linear regression plots, error plots, and smoothed and fitted curves.

Finally, Axum comes with its own programming language that has many similarities with C. This allows the user to customize the data analysis by programming specific functions which can subsequently be accessed in the same way as built-in Axum functions. The user can also create scripts to automate a series of manipulation steps allowing speedy analysis of multiple data sets.

The program can be quickly learned to perform rudimentary commands such as graph generation or standard data analysis, especially by users who have experience with other icon-driven programs. The available help is quite good and includes a tutorial, standard on-line help, examples, templates, and the 370-page manual. However, there are levels of complexity to Axum that are only fully appreciated with time and experience. This is true of the programming language for data analysis for which there might be a relatively steep learning curve, especially for the user who is not already an expert on C programming.

Susan B. Sinnott, *The University of Kentucky*

JA975902N

S0002-7863(97)05902-7

Book Reviews *

Thermal Characterization of Polymeric Materials. Second Edition Volumes 1 and 2. Edited by Edith A. Turi (Polytechnic University, New York). Academic Press: San Diego. 1997. xxiv + 2420 pp. ISBN 0-12-703783-7.

This is the second edition of a book which brings us a systematic and disciplined contribution by the same editor and many of the same authors as the text first published in 1981. In the intervening sixteen years, thermal analysis (TA) has become the most widely used approach to polymer characterization, and 40 000 papers related to this field have been published. Not surprisingly, the first book has grown in size from 970 pages to a set of two volumes and over 2500 pages. Yet the editors and authors have successfully carried out their colossal undertaking and produced a text that is both comprehensive and tightly written, with thoroughly updated information on theory, applications, and instrumentation. It will no doubt be widely used as a reference in chemistry, chemical engineering, and material science.

The ten chapters, written by eleven contributors, range in length from 135 to 490 pages. The first two, Thermoanalytical Instrumentation, Techniques, and Methodology (P. K. Gallagher) and The Basis of Thermal Analysis (B. Wunderlich) introduce the remaining chapters respectively devoted to thermoplastic polymers, polymer blends and block copolymers, elastomers, thermosets, fibers, films, composites, and additives to polymers. There are over 1000 figures. Each chapter contains an extensive though selective list of references that, for the most part, are very up-to-date. Each also includes its own list of acronyms, abbreviations, and symbols and can be read as a self-contained monograph or treatise, although Chapters 7 and 8 (Fibers and Films, both written by the same three authors) are complementary.

The two introductory chapters also complement one another to some extent, without duplication of information. They present a comprehensive overview of the central techniques of TA: thermometry; dilatometry; the various forms of thermomechanical and dielectric analysis; calorimetry, including differential thermal analysis and

differential scanning calorimetry (DSC); and thermogravimetry. Chapter 1 provides a description of instrumentation and procedures for these and other techniques, such as emanation and evolved gas analysis, thermally stimulated current analysis, thermoacoustimetry, and thermosonimetry. Advances in data acquisition and robotics are presented. Recent modifications to conventional TA (such as modulated DSC or "controlled rate" TA) are described. The second chapter provides the theoretical underpinning for the central techniques of thermal analysis as well as a link between molecular structure and motion (including some aspects of molecular dynamics simulation) and the macroscopic variables used in thermal methods. This chapter could well be used as an introductory thermodynamics text, with its clear overview of equilibrium and irreversible thermodynamics, kinetics, and phase behavior.

Numerous examples of the complementary or simultaneous use of various characterization techniques—including the use of TA combined with spectroscopic techniques—are scattered throughout the book, illustrating the ubiquitous presence of thermal analysis in research, development, quality control, and production.

Some degree of overlap between chapters is unavoidable in the framework of such a vast undertaking. One can cite for example discussion of thermoplastic elastomers which are examined in the chapter on Polymer Blends and Block Copolymers, with emphasis on their morphological and thermodynamic behavior, and again in the chapter on Elastomers, with emphasis on structure property correlations. One can similarly mention the use of thermal data for analysis of cure kinetics; the topic is again addressed in two different chapters, but again with different emphasis. Actual duplication of information is remarkably minimal, a tribute to the disciplined team approach fostered by the editor.

Rita B. Blumstein, *University of Massachusetts, Lowell*

JA975533V

S0002-7863(97)05533-9

*Unsigned book reviews are by the Book Review Editor.

Calcium Hypothesis of Aging and Dementia. Edited by John F. Disterhoft (Northwestern University Medical School), William H. Gispen (Rudolph Magnus Institute), Jorg Traber (Tropenwerke, GmbH), and Zaven S. Khachaturian (National Institute on Aging, NIH). *Annals of the New York Academy of Sciences*: New York, 1995. 482 pp. \$130.00. ISBN 0-89766-878-2.

This book is the result of a meeting on the Calcium Hypothesis of Aging and Dementia which was held on the campus of the National Institutes of Health in Bethesda, MD, on December 15–17, 1993. The book presents the work of leading scientists to advance the understanding of the role of calcium on the aging process and in the development of neural states of dementia. It examines the slight imbalances of calcium, which, sustained over a long period, could lead to cellular deterioration and ultimately death, and presents reviews ranging from considerations of calcium channel function at the molecular level to the role of altered calcium levels in behavior.

JA9656154

S0002-7863(96)05615-6

Development and Validation of Analytical Methods. Edited by Christopher M. Riley (Du Pont Merck Pharmaceutical Co.) and Thomas W. Rosanske (Hoechst Marion Roussel, Inc.). Elsevier: Oxford, U.K., 1996. x + 352 pp. \$88.00. ISBN 0-08-0427928.

This is a very important reference book for anyone that needs to meet regulatory requirements for analytical methods, in terms of methods development, optimization, and especially validation. Any analyst working in a pharmaceutical or biotechnology company, analytical service laboratory, government regulatory laboratory, or outside laboratory working for any of the above organizations must eventually learn about many of the topics contained within this book. In chapters in a previous publication by Riley, Lough, and Wainer, entitled *Pharmaceutical and Biomedical Applications of Liquid Chromatography* (Pergamon Press, Elsevier, 1994), an orientation toward methods development, and to some extent, validation were also covered. The current book attempts, and at times succeeds, to turn its attention more to method validation, and well as contains some chapters on method development and optimization. In our teaching of this subject matter via various short courses, workshops, tutorials, and undergraduate and graduate formal courses at a university, it is clear that there is a tremendous interest and a need to learn the very subject matter of this text. The question is whether or not this book really does discuss, in the main, method development and validation of analytical methods?

There is no question but that this subject is vitally important to a large segment of the chemical community, especially analytical chemists involved in any regulated environment. There is a crying need within academia to learn more about method validation, especially when we are training analytical chemists to work in private industry or government laboratories. During most academic preparation, the students are never even introduced to the basic subject matter, at either the undergraduate or graduate level. Though there are numerous texts and review papers that appear on a regular basis involving analytical chemistry, HPLC, HPCE, mass spectrometry, and other analytical areas, most of these do not even introduce the subject matter of the current text. At the graduate level, virtually no analytical courses cover this subject matter either. At the undergraduate level, usually less is discussed about method validation than any other subject in the analytical chemistry curriculum. Why is that the case today? This book attempts to address this dire lack of attention, concern, education, and learning. There are very few books, in part or whole, that really discuss, in depth, the basic subject matter of validation for analytical methods. It is as if this is not a subject matter worthy of discussion in a formal analytical chemistry text nor course. How can we overlook such a terribly important and vital subject until the time comes when we must actually validate a method ourselves for the FDA, EPA, or another regulatory authority?

This book certainly fills a basic need in this area; however, it has some basic flaws, not the least of which is that it does not really discuss

method validation the way that it could and perhaps should be discussed. At the same time, there are perhaps chapters in the book that are out of place, such as Chapter 2 on statistical parameters and analytical figures of merit, which are perhaps better found in a general analytical chemistry text, rather than one devoted to analytical method development and validation. Though Chapter 1 does discuss assay validation and interlaboratory transfer, it does so without going into the basic, specific (individual) techniques involved in true method validation. It also does not lead the reader through the process of different levels of validation at different stages of the drug development life cycle or of an analytical method's utility at a given time/place. Chapter 1 should have been the very heart of the book, yet it is given less than a total of 12 pages. On the other hand, the chapter on statistical parameters and analytical figures of merit is given a total of almost 60 pages. There should have been a reversal in the page allocation for these first two chapters.

The next section, Part Two: Regulatory Considerations, consisting of Chapters 3–5, deals with an overview of current, worldwide regulations involving analytical methods validation. However, not enough emphasis is placed on the current, up-to-date International Conference on Harmonization (ICH) guidelines. The ICH guidelines are about to supplant virtually all other government regulatory guidelines in the pharmaceutical area and may (it appears today) eventually be adopted by our USP with full FDA sanctions. Thus, at least one entire chapter on ICH alone might have been apropos for a book of this type and scope. The other two chapters in this Part Two are devoted to the Barr decision, which together consist of about 30 pages. These chapters could be considered irrelevant to the scope and intent of the book. The Barr decision does not relate to analytical method development, optimization, nor validation, but rather to the use of analytical statistics and good laboratory practices in a pharmaceutical laboratory environment.

Part Three has chapters that deal with bulk drug substances and finished products, dissolution studies, robotics and automatic workstations, biotechnology products, biological samples, analytical methods for cleaning procedures, and computer systems and computer-aided validation. These chapters discuss the development of analytical methods and their optimization for various types of samples and pharmaceutical products or processes. They do not, by and large, deal with method validation for any of these products or processes or stages of a drug's development. Though the USP guidelines for method validation are mentioned at various places in Part Three, there is not enough discussion of each parameter. In addition, there is no logical, sequential order of when/where/how to demonstrate each of the USP figures of merit for method validation, nor how much USP method validation is required as a function of the stage of the drug development process.

Of all the chapters in Part Three, perhaps the best was that by Srivatsa dealing with biotechnology products. In this chapter, he discusses the basic biopharmaceutical industry, specific regulatory requirements of biopharmaceuticals, analytical requirements of biopharmaceuticals, and validation of various analytical biotechnology techniques. This is an excellent overview of the basic biotechnology industry, with emphasis on the types of methods that need to be developed, but again with very little discussion of method validation, per se.

The references, by and large, are very up-to-date, thorough, complete, on-target, and comprehensive. We suspect, however, given the title, that the reader may expect more basic validation procedural information than what has been provided. However, the book accomplishes its goal of discussing issues that need to be considered and serves as a guide to considerations that must be attended to in any analytical process. In this regard, these reviewers consider the book a valuable resource for those working in a regulated environment.

Ira S. Krull, *Northeastern University*Michael E. Swartz, *Waters Corp.*

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