Topical Techniques

Contemporary Instrumental Analysis. By *Kenneth A. Rubinson* and *Judith Faye Rubinson.* Prentice Hall, Upper Saddle River 1999. xx+840 pp., hardcover $ 101.20.—ISBN 0-13-790726-5

Reviewing a textbook is often not a pleasant thing for me to do, because I end up being only half convinced about the quality and I find myself looking for reasons why and searching for mistakes. Not in this case: it was immediately clear to me that the text *Contemporary Instrumental Analysis* by Kenneth A. Rubinson and J. Faye Rubinson is a high-quality book, a pleasure to read, written with great care, and produced to a high standard.

The choice of topics covered by this book is quite classical (statistics, sampling, electrochemical methods, elemental analyses, spectroscopic methods, separation methods, kinetic methods), but it is a textbook targeting undergraduate students who need to have a good foundation in analytical chemistry. Many more topics could have been covered, for example, more on surface analytical methods, scanning probe microscopy, or quality assurance. However, I think that the authors made a good choice of topics and they did include chapters that are often neglected but important and basic, for example the chapter on sampling (Chapter 3) or that on electroseparations (Chapter 16). The material presented is free of mistakes and, as the title promises, up-to-date. The concepts are explained in a straightforward, easy-to-follow fashion.

What I found very attractive are the beautiful graphics, an excellent collection of original literature citations, special subchapters offering a "deeper look" into selected topics, and problems (with solutions) at the end of every chapter. The "case studies" to illustrate applications of paricular analytical techniques are very well chosen and fun. Examples of "case studies" that caught my eye include a page on "atmospheric archives" in sand dunes, which addresses the problem of sampling for environmental analyses; the one on the alpha proton X-ray spectrometer carried by the Mars rover to analyze the elemental composition of Martian soil and rocks near the landing site of the Pathfinder mission; a page on detection of steroid abuse in athletes by chromatographic methods; and many others, all with references to the original literature. These examples are not only fascinating and motivating for students but are valuable material to draw from for teachers of analytical chemistry.

The book includes many tables, numerical examples, a good index, and seven appendices with information on statistics, standard solutions, detection limits, standard and formal electron potentials, solvent miscibility, formula weights, and a list of acronyms.

Overall, I can highly recommend this book as a textbook for undergraduate courses in analytical chemistry both for students and for teachers, and as a quick reference book for professionals.

Renato Zenobi
Department of Chemistry
ETH Zentrum Zürich (Switzerland)

Comprehensive Natural Products Chemistry. Vol. 1-9. Edited by *Sir Derek Barton, Koji Nakanishi,* and *Otto Meth-Cohn.* Elsevier Science Ltd., Amsterdam 1999. 9 x xl + 8.500 pp., hardcover ca. 2956 Euro (3,755 $).—ISBN 0-08-042709-X

"For many decades, Natural Products Chemistry has been the principal driving force for progress in Organic Chemistry." This is the sentence with which the editors of Comprehensive Natural products Chemistry (CNPC) begin their introduction, and most organic chemists will intuitively and emphatically agree. This includes even those who are unable to give a clear answer to the question: "Where does natural products chemistry stand at the beginning of the 21st century?".

Those interested in this difficult but highly up-to-date question will highly appreciate the publication of CNPC. For years there has been the need for a relevant work representing the current state of knowledge and the perspectives of modern natural products research in a comprised form on a level higher than a mere textbook. This gap is filled indeed by CNPC in an outstanding way.

This work, initiated and edited by some "top stars" of natural products chemistry, comprises eight volumes, each of which contains an author and a subject index. Additionally, volume 9 contains a thoroughly composed overall index. In the 136 chapters, which have been written by internationally renowned experts, the most varying aspects of modern natural products chemistry are addressed and presented within a scientific context. The amplitude of the subject has been structured as follows:

Volume 1: Polyketides and Other Secondary Metabolites Including Fatty Acids and Their Derivatives.

Volume 2: Isoprenoids Including Carotenoids and Steroids.

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Volume 3: Carbohydrates and Their Derivatives Including Tannins, Cellulose, and Related Lignins.
Volume 4: Amino Acids, Peptides, Porphyrins, and Alkaloids.
Volume 5: Enzymes, Enzyme Mechanisms, Proteins and Aspects of NO Chemistry.
Volume 6: Prebiotic Chemistry, Molecular Fossils, Nucleosides, and RNA.
Volume 7: DNA and Aspects of Molecular Biology.
Volume 8: Miscellaneous Natural Products Including Marine Natural Products, Pheromones, Plant Hormones, and Aspects of Ecology.
Volume 9: Cumulative Indexes.

Each volume has the same 40 page preface by K. Nakanishi, which not only sketches and explains the concept and the structure of the complete works, but at the same time sketches an extremely readable historical perspective of natural products chemistry. It also includes a two-page obituary by A. I. Scott for the co-editor Sir Derek Barton, who passed away on March 16th 1998, i.e. before the completion of the works.

The title of the work should not be misinterpreted: CNPC is in no way whatsoever an encyclopedia of natural products suitable for the directed search for information on structure, transformation or biological activity of a particular natural product. To do so, one is to consult other works or the renowned online databases.

Comprehensive Natural Products Chemistry completely lives up to its title in a different aspect. It draws an extensive bow over natural products chemistry in its original sense, i.e. it treats low molecular weight natural products (secondary metabolites) and biopolymers equally. Following the motto "How does nature actually make all these molecules of life?", the vast area of natural products chemistry has been organized not by structure, but in terms of biosynthesis. In consideration of aspects of biochemistry and molecular biology, contexts are worked out, the interplay of natural products chemistry with neighboring disciplines such as biology and chemical ecology is pointed out, and perspectives for future developments are sketched.

This monumental work is a genuine repertory and each chapter offers an excellently researched and easily readable summary of important branches. Due to the careful design, processing and quality of print (sporadically even in color), it is a real pleasure to browse through the CNPC volumes. Trying to systematically cater to each volume and chapter would go beyond the scope of this review. It is possible though to look up details of the table of contents (headings and authors of all chapters) on the internet at www.elsevier.com/inca/publications/store/6/0/0/3/8/5/.

Even though aspects of chemical synthesis are dealt with in this work only sporadically, the lecture (of at least of some of the volumes) of CNPC will be profitable in particular for chemists specialized in the synthesis of natural products. They possibly could not only carry away valuable impulses for the choice of relevant target structures, but – and this is surely a more crucial aspect – could also be encouraged to approach and grapple with the more biologically orientated neighboring disciplines of chemical synthesis. It is easy to foresee that in the future the supply of economically important (i.e. complex) natural products will rely more and more on chemoenzymatic methods. To do so, biotechnology and organic synthesis have to converge to a larger extent. In this sense, CNPC sort of fulfills a cultural mandate, as it opens up (not only to synthetic chemists) an ideal introduction to the study of pathways and mechanisms of biosynthesis. In doing so, it also creates a feel for the variety of enzymatic transformations besides giving an insight into the structural diversity of natural products.

With all due enthusiasm for the altogether extraordinary conception and quality of CNPC, it must not be ignored that such a work has to meet natural limits. The user has to be aware that he will not find that all aspects of natural products chemistry are covered. For example, the title of Volume 6 (Prebiotic Chemistry, Molecular Fossils, Nucleosides and RNA) may raise expectations, which then will not be met. One will in vain search for works by Orgel, Eschenmoser, or Kiedrowski, but one will be compensated with a panoramic view on the world of RNA, going from RNA structure motifs over the chemical synthesis of RNA to the various aspects of ribozymes.

It is unavoidable that many natural products chemist will find that their personal hobbyhorse has not been taken duly into consideration. And with regard to the immense size of the work it would be finical to criticize the few errors and wrong formulae, which have crept into the work in spite of all the editors' diligence. The excellent overall impression left behind by the work is hard to upset.

All in all, Comprehensive Natural Products Chemistry is an extremely felicitous, brilliantly edited, and highly welcome work, which must not be missing in any chemical library. It does not only mark off the status and philosophy of the research on natural products at the end of the 20th century, but creates awareness for the increasing importance of interdisciplinary research. CNPC surely will have an impact on future generations of natural products chemists, as the work mirrors the immense fascination and driving power which definitely will emanate from natural products chemistry in years to come.

Hans-Günther Schmalz
Institut für Organische Chemie
Universität Köln (Germany)

Molecular Descriptors in QSAR/QSPR. By *Mati Karelson*. Wiley-Interscience, New York 2000. x+430 pp., hardcover DM 398.00.—ISBN 0-471-35168-7

The virtual screening of large libraries of compounds with the object of finding new active agents for pharmacology and plant protection and predicting their bioavailability is one of the great tasks of modern times, as also is the scientifically based evaluation of tens of thousands of "old" substances, i.e., those that are already in commercial use but have not yet been sufficiently tested with regard to their possible toxicity and ecotoxicity. One approach to this is the use of statistical models based on QSAR (quantitative structure – activity relationships) and QSPR (quantitative structure – property relationships). With

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these one attempts to discover relationships between different properties. This involves choosing a chemically related series of compounds and searching for quantitative correlations between their physicochemical, geometrical, topological, or quantum-mechanical descriptors and their biological properties. The resulting model is validated by testing the quality of its predictions within the series, and is then used to predict the biological properties of other compounds. For this procedure it is essential to have measured values of physicochemical properties or to be able to calculate molecular descriptors for the compounds whose biological activity one wishes to predict using the model.

That problem is the subject of this book by Karelson. About 130 pages of the book (with 500 literature references) are devoted to examining different physicochemical descriptors, such as those describing inductive electronic properties and resonance parameters (σm, σp, σ^*, σI, F, σ^+, σ^-, σR, R, R^+, and R^-), steric parameters (various Es values), and the molar refraction MR. The values of these quantities for the most important substituents are listed in tables. This section of the book also includes details of various solvation parameters, but in this case for individual compounds, not for substituents. Lipophilicity is discussed only very briefly, listing only the values of the octanol–water partition coefficient P and the lipophilicity coefficient π (tables for 189 substituents). Unfortunately there is no discussion about the dependence of π on the position and nature of the substituents (*meta*, *para*, aliphatic), nor are there any data for partition in systems other than octanol–water, which are important in relation to problems such as estimating the flow of blood to the brain.

The second section (240 pp., with 900 literature references) is concerned with the calculation of theoretical descriptors, which can be classified as constitutional, geometric, topological, electrostatic, quantum-chemical, thermodynamic, or combined. Constitutional, geometric, and topological parameters describe the chemical similarity between the molecules of a series, and are therefore in principle well suited for QSAR/QSPR modeling. Quantum-chemical parameters provide useful information about the interaction of a ligand with the biological target molecules. However, these parameters are too often used in a blind manner and large numbers are combined together, with the result that the models thus derived are usually of no biological relevance. The only ways of avoiding this are by cross-validation in groups, or by repeated random mixing of the dependent variables (scrambling) to make sure that such a procedure cannot produce other similarly "good" models.

There is a useful short section describing methods for deriving QSAR/QSPR models, with over 80 literature references; the methods include multiple linear regression analysis and principal components analysis. A CD-ROM accompanying the book contains an electronic version of the most important tables of parameters in the book (a set of five σ values for 271 different substituents, six resonance parameters for 191 substituents, three steric coefficients of the molar refraction MR for 109 substituents, and several solvation parameters for 63 compounds), programs for calculating many kinds of geometric and topological descriptors, and (in case results from a semiempirical calculation are available) a program for calculating various quantum-mechanical parameters. For these one needs to input MDL*.mol files (for geometrical parameters) or MOPAC*.mno files (for quantum-mechanical parameters). The software can be run with a number of operating systems, including Windows 98 and earlier versions. With a good deal of effort, using a poorly explained procedure, one can assemble these data in a single table and then subject them to a multiple regression analysis. Nevertheless, this program (based on the CODESSA software) is surprisingly powerful and quick. Even in difficult cases (such as the notorious Selwood data set), it gives good results in a relatively short time.

The book is suitable for scientists who are seeking an initial overview of the use of physicochemical and topological parameters in investigating structure–property relationships. The many well chosen examples illustrate the practical use of the various descriptors. However, as many of the descriptors that relate to ligand–protein interactions (lipophilicity, molar refraction, Verloop parameters, hydrogen-bonding descriptors, etc.) are only covered rather briefly, the book is less suitable for applications in pharmaceutical chemistry, plant protection, and ecotoxicology.

Hugo Kubinyi
BASF AG
Ludwigshafen (Germany)

Clean Synthesis using Porous Inorganic Solid Catalysts and Supported Reagents. By *James H. Clark* and *Christopher N. Rhodes.* (Series: RSC Clean Technology Monographs.) Royal Society of Chemistry, Cambridge 2000. x+108 pp., hardcover £ 55.00.—ISBN 0-85404-526-0

"Clean synthesis" is a catchword that deserves to be heeded and put into practice. But exactly what are clean syntheses? Obviously they are syntheses that conserve energy and resources and produce no wastes. To that extent the promise implied by the title of this third volume in the series *RSC Clean Technology Monographs* is misleading. One cannot simply argue that no definition was available. The use of porous solid inorganic catalysts and supported reagents mentioned in the rest of the title only gives waste-free syntheses in exceptional cases, and the preparation of the materials for such reactions is not usually economical in either energy or resources. At best one can only talk of a "cleaner synthesis", and even then only after comparison with alternatives that have been tested, and that is certainly not what is intended. In the preface, for example, we find the sweeping statement that stoichiometric processes should be replaced by catalytic processes in order to minimize wastes. The benefits of catalysis have never been disputed, but there have been successes in developing waste-free stoichiometric reactions, for example, in organic solid-state chemistry, without the use of catalysts. These should not be ignored, since with 100% yields they are truly "clean". Furthermore, we can assume that the chemical industry has for many years been developing its technology to be as "clean" as possible. Therefore, proclaiming a "clean technology revolution" is inappropriate now.

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If one leaves aside the overstated claim in the title (which is reiterated frequently in the text, but, in contrast, with only three references to "cleaner" methods), this short monograph certainly has its positive aspects, since there are countless numbers of research groups working on this theme. For these groups the book describes the properties of some of the "more useful" catalysts and supported reagents, and those applications to liquid-phase reactions that the authors regard as the most "interesting and valuable". Naturally, however, the choice must be subjective on a total of 102 pages of text.

Of the four chapters, the first is an introduction, and the following three are devoted to zeolites, clays, and supported reagents. They contain useful information for the newcomer to the field, but also for those with some experience. The results described here will serve to show how much further improvement is still needed, as these never achieve 100% yields (although the authors avoid setting that as a requirement).

The introduction (Ch. 1) explains some elementary concepts related to heterogeneous reactions. Chapter 2 lists 11 technical processes using zeolites. For data on reaction conditions and yields one has to consult the cited literature in most cases; no patent references are given. The majority are gas-phase reactions, but some liquid-phase reactions are also described. However, with the best will in the world one cannot describe the latter as "clean", as can be seen from the example of the production of 4-hydroxyacetophenone from phenyl acetate using Faujasite H-USY with phenol as the solvent at 150 °C, which gives 40% conversion and a yield of 80%.

Chapter 3 describes how clays in the form of layer silicates can be modified by preparation of "pillars" and used in acid and metal catalysis. Eight types of reactions for producing bulk chemicals are mentioned, but no details of patents or currently operating industrial processes are given. A consequence of ignoring the patent literature is that the cited publications are treated uncritically, and this detracts from the book's declared aims. For example, with regard to the reaction shown in Figure 3.5 (aniline and formaldehyde with Kaolinite at R.T.), neither the authors nor Reference 36 mention US Patent 4071558, which describes in detail the synthesis of the intermediate 4,4'-diaminodiphenylmethane and the distribution of the products (regioisomers together with oligomers and polymers) for temperatures in the range 80–300 °C and using acid-activated clay. The authors of the book present a much simpler picture, claiming that the reaction gives exclusively the desired product in 96% yield. This reviewer went to the trouble of testing the claim, and found that under the published conditions the reaction was incomplete using kaolinite and, as expected, gave hexahydro-1,3,5-triphenyltriazine and other products, but no trace of 4,4′-diaminodiphenylmethane.

With regard to the idea of agricultural products in the form of substances on clay supports, the enormous energy requirement for pretreatment of the clay and for microwave irradiation must raise doubts about the economics of the scheme.

The largest part of the book, Chapter 4, is mainly devoted to catalysts, whereas reagents on inorganic supports are treated in less detail. The main types of catalysts discussed are silica gels, structured silicates, montmorillonites, aluminum oxides, zeolites, activated carbon, and calcium fluoride. Then, after some general comments about the preparation and properties of supported reagents, the authors discuss their use for oxidations, alkylations, condensations, substitutions, and aminations, and describe some selected examples. Here again, yields are not usually given; where they are given they never reach 100%. In view of the difficulties experienced with supported reagents, one has to ask the question: what is "clean" about them? It is not enough to show that, with considerable effort and expense, one might achieve a small increase in yield.

Errors in the formulas and other deficiencies were noticed on pages 19, 26, 34, 40, 51, 82, and 88. Also, throughout the book, the bonding to the supports should have been shown correctly (e.g., in Fig. 4.2 and nine other figures; however, the Si–C bonds are shown correctly for the Grignard reaction in Fig. 4.26). Admittedly this is only a short monograph, but it does not convey a detailed picture of the complexity of solid catalysts.

The literature references given at the end of the chapters amount to 360 in total. The four-page subject index is incomplete (many important keywords are missing, e.g., "reduction"). If an author index had been provided it would have been useful by showing any bias in the choice of topics.

The outlook for environmentally friendly methods of synthesis would indeed be bad if the possibilities were limited to what is discussed here, and if there were no examples of waste-free syntheses with a 100% yield (which are not mentioned anywhere in this book). In fact, the prospects for "cleaner synthesis" are considerably better than shown here. This short monograph fails to live up to the expectations raised by the title. That is regrettable, as this is an extensive field of research which has the potential for further growth. Up-to-date evidence for that can be seen in 4487, 29255, and 1309 entries in File CA of *Chemical Abstracts*, which resulted from a search combining the keywords clay, zeolite(s), and supported reagent(s), together with "catalysis or catalyst(s)", respectively. Despite the fact that this is the third volume in a series from the Royal Society of Chemistry, numerous libraries will not pay £ 55.00 for this book of 108 pages.

Gerd Kaupp
Institut für Organische Chemie I
Universität Oldenburg (Germany)

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