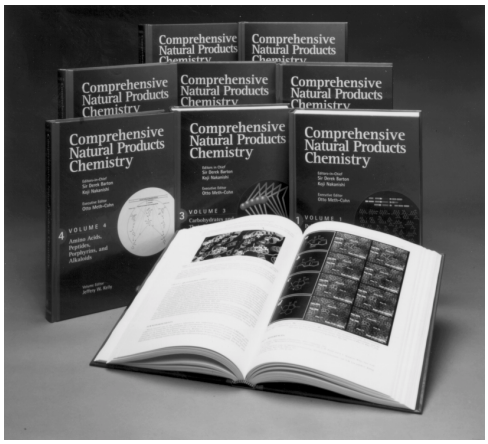
Comprehensive Natural Products Chemistry, Edited by D. H. R. Barton† and K. Nakanishi. Elsevier, 1999. ISBN 0-08-042709-X, $3744.



The Pergamon Press comprehensive chemistry surveys have performed a valuable service to our profession. Comprehensive Organometallic Chemistry, Comprehensive Organic Synthesis and Comprehensive Heterocyclic Chemistry all set a high standard for taut organisation, balance, judicious choice of contributors, and very clear guidelines. The latest addition to the series is Comprehensive Natural Product Chemistry (CNPC) edited by Otto Meth-Cohn, Koji Nakanishi and the late Sir Derek Barton. Compared with its forebears, natural products chemistry is a more intractable subject and less amenable to comprehensive treatment. The editors wisely chose to reduce the material to more manageable proportions by focusing on biosynthesis. In general, biological activity, structure determination, and synthesis are relegated to the cellars of the subject.

The pioneers in biosynthesis were primarily concerned with structure elucidation of secondary metabolites and biogenetic theory emerged as a tool for structure elucidation The advent of isotopic labelling and NMR spectroscopy engendered a new era of refinement where biogenetic theories were affirmed or rejected and new and unusual pathways discovered. However, in recent years the focus has shifted away from the end product of a biosynthetic sequence to its genetic instruction set and the intervening enzymatic machinery. Consequently, biosynthetic research is now a complex amalgam of molecular biology, genetics, biochemistry and enzymology with a shift in emphasis to primary metabolism. One of the strengths of CNPC is that it tries to embrace the whole gamut of biosynthesis from DNA to end product.

Before I survey each of the separate volumes, a few comments about the work as a whole are in order. The production values are generally good with clear organisation and clear structures done to a common standard. On the rare occasions when authors deviated from the guidelines, the results are regrettable as in chapter 9, volume 1. The occasional use of colour photographs was welcome and illuminating. As an overture, Koji Nakanishi provided a concise and authoritative introductory essay to the series entitled "An Historical Perspective of Natural Products Chemistry". Curiously, this essay was duplicated at the beginning of all the volumes including the indexes. Each volume has an introductory chapter by the volume editor, which gives an overview of the volume, and each volume ends with an author and subject index. The overviews vary widely in length (from 1 to 22 pages), quality and usefulness and none match up to the distillation afforded by Alan Katritzky's single-handed overview of all of Comprehensive Heterocyclic Chemistry.

The biosynthesis of natural products chemistry was covered by ca 250 authors in 136 chapters divided into 8 volumes with a ninth volume of cumulative indexes. In he following paragraphs the contents of the individual volumes will be summarised together with some pertinent comments.

Volume 1 edited by Ushio Sankawa (31 chapters, 1007 pages,): Polyketides and Other Secondary Metabolites Including Fatty Acids and Their Derivatives. This volume is quite a heterogeneous collection consisting of chapters on the biosynthesis of compound classes (fatty acids, eicosonoids, coumarins, flavonoids, isoflavonoids, chalcones, stilbenes, lignins) as well as detailed treatment of specific compounds such as aflatoxin, cyclosporin, the enediyne antibiotics, 6-methylsalicylic acid, bialaphos and fosfomycin. The shikimate pathway and macrolides biosynthesis were given a detailed and satisfying enzymological treatment. A chapter on structure, function, and engineering of bacterial aromatic polyketide synthases by Richardson and Khosla together with the chapter on biosynthesis of erythromycin and related antibiotics by Staunton and Wilkinson deserve special mention because the authors show how detailed knowledge of a biosynthetic pathway can create opportunities for harnessing the genetics and machinery of nature to produce novel compounds.

Volume 2 edited by David Cane (14 chapters, 446 pages): Isoprenoids Including Carotenoids and Steroids. Organic chemists have probably lavished more attention on the isoprenoids than any other class of natural product. They have a good public image (benign and useful) and a diversity of architecture which has inspired biosynthetic and synthetic chemists in equal measure. Given their rich history, it may seem surprising that volume 2 should be so slight. However, rather than produce elaborate metabolic pathway charts classifying the isoprenoids by structure, the contributors have focused on the enzymology of isoprenoid biosynthesis and in a few cases whole chapter were dedicated to a single enzyme such as squalene synthase and squalene epoxidase. Whether by accident or design, the contributors to this volume displayed a welcome consistency of approach. The final chapter in the volume on ginkolide biosynthesis by Schwarz and Arigoni is a

splendid evocation of the insight and ingenuity that can be gleaned from classical labelling studies.

Volume 3 edited by B. Mario Pinto (20 chapters, 939 pages): Carbohydrates and Their Derivatives Including Tannins, Cellulose, and Related Lignins. The third volume deals with the biosynthesis of glycoconjugates. There are 4 sections with the first section dealing with glycoproteins, glycolipids and proteoglycans that mediate biorecognition. The second section concerns glycoconjugates of importance to protozoa and bacteria including lipopolysaccharides, peptidoglycans, and glycosylphosphatidylinositol anchors. Part 3 deals with the occurrence, genetics and biosynthesis of deoxysugars and a comprehensive survey of aldolases that might find synthetic utility. The final section surveys the carbohydrate derivatives of importance in energy storage (starch and glycogen), structure (cellulose) and protection (lignins and tannins).

Volume 4 edited by Jeffery W. Kelly (14 chapters, 429 pages): Amino Acids, Peptides, Porphyrins, and Alkaloids. Volume 4 is the runt of the litter. It is a collection of special topics some of which really belong elsewhere. For example, the chapter on protein palmitoylation is ill at ease in the company of its fellows and the chapter on glycosylphosphatidylinositol-anchor biosynthesis duplicates a chapter covered in volume 3. Worst of all is the meagre coverage given to alkaloid biosynthesis—two chapters covering a mere 66 pages. By contrast, the biosynthesis of lignin was covered in 130 pages in volume 3. But there are also some fine things in this volume. The biosynthesis of heme by Shooligin-Jordan and Scott's review of enzymatically controlled steps in vitamin B12 biosynthesis provide useful summaries by major exponents of the field. The biosynthesis of β-lactam compounds from micro-organisms is accompanied by a separate chapter by Luengo on the enzymatic synthesis of penicillins which again offers a glimpse into the future of organic synthesis. Two chapters are also devoted to peptide synthetases.

Volume 5 edited by C. Dale Poulter (17 chapters, 495 pages): Enzymes, Enzyme Mechanisms, Proteins, and Aspects of NO Chemistry. With volume 5 there is a shift in gear. The previous volumes were primarily concerned with secondary metabolites—natural products which are species-genus-family specific together with their associated enzymology. By contrast volume 5 engages the enzymatic machinery of more universal primary metabolism. Each chapter deals with specific reactions (e.g. nucleophilic epoxide opening, ester hydrolysis) or specific enzymes (e.g., phosphatases, glycosyl transferases, dehalogenases). A chapter on catalytic antibodies completes the volume. The two pages devoted to the reaction of tyrosine with NO hardly warrant "Aspects of NO Chemistry" in the title of volume 5.

Volume 6 edited by Dieter Söll, Susumu Nishimura and Peter B. Moore (299 pages): Prebiotic Chemistry, Molecular Fossils, Nucleosides and RNA. Volume 6 is about the Cinderella of the biopolymers, RNA. The discovery that RNA is no mere molecular shuttle of genetic information but a molecule possessing catalytic activity in its own right, together with the major advances in the sequencing and synthesis of RNAs, has stimulated intense interest which is concisely summarised here. The full panoply of topics are covered including chapters on structure (NMR and X-ray), conformation, thermodynamics, metabolism and mechanism of action. There is also a brief but welcome chapter on the chemical synthesis of RNA. Like volume 5, volume 6 promises rather more in the title than is actually delivered. The closest this volume got to a molecular fossil was me and prebiotic chemistry is only tangentially covered.

Volume 7 edited by Eric T. Kool (18 chapters, 733 pages): DNA and Aspects of Molecular Biology. Volume 7 has steered an admirable course through the shoals of compression and relevance. Its length in relation to volume 6 reflects the greater emphasis DNA has enjoyed but even at 733 pages, a great deal was omitted. The volume divides into 4 sections. The first section (4 chapters) describes in detail the physical properties of DNA including NMR methods. The second section comprising 7 chapters is concerned with various aspects of DNA chemistry including a concise and discriminating discussion of chemical synthesis by Iyer and Beaucage. Several chapters deal with the design, synthesis and practical applications of analogues and topological variants and the section concludes with a discussion of DNA damage. The third section (5 chapters) covers molecules that bind to DNA and the final section (2 chapters) focuses on techniques from molecular biology (PCR amplification and cloning) that have been central to the revolution in biosynthetic research.

Volume 8 edited by Kenji Mori (7 chapters, 749 pages): Miscellaneous Natural Products Including Marine Natural Products, Pheromones, Plant Hormones, and Aspects of Ecology. With volume 8 we come full circle to the natural end products of metabolism and the title is an accurate reflection of the contents.

Volume 9 (351 pages): Cumulative Indexes including a Formula Index compiled by John Newton and a Subject Index compiled by Philip and Lesley Aslett. The subject indexes from the preceding 8 volumes were combined but the author indexes were not. A formula index was included in volume 9 which was omitted from the individual volumes. Unfortunately pages 131-162 were missing from my copy of the indexes. A browse through the formula index brought to light one amusing entry: the reader will be pleased to know that water has a single entry in volume 5, p 79.

I have enjoyed my trawl through Comprehensive Natural Products Chemistry and I certainly found it useful and that, in the end, was its purpose. As with any multi-author work covering such a vast subject, there were peaks and troughs. Some of the peaks were very high and none of the troughs were abysmal. No doubt longer acquaintance would reveal further blessings and blemishes. Taken together, the editors and authors have managed to impose a

logic and order on a very unwieldy subject which is in rapid transition.

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Metallocenes, A. Togni and R.L.Haltermann, Eds, Wiley-VCH, 1998, pp.790, DM 398, ISBN 3-527-29539-9.

This two-volume set is the companion to "Ferrocenes: Homogeneous Catalysis; Organic Synthesis; Materials Science" (A.Togni and T.Hayashi, Ed.'s, VCH, 1995). Each of the twelve chapters covers a specific area of metallocene chemistry and is written by acknowledged experts in the field. Volume 1 is sub-titled "Synthesis and Reactivity" and contains Chapters 1-8. The remaining four chapters are included under the heading "Applications" in the much smaller Volume 2.

The editors have adopted the widest possible interpretation of the term "metallocene". Not only are sandwich compounds having the general formula $[M(\eta^5\text{-}C_5R_5)_2]$ to be discussed, "bent metallocenes" (e.g. $[W(\eta^5\text{-}C_5H_5)_2H_2]$) and even *mono*cyclopentadienyl derivatives are also to be included. The authors of individual chapters have, however, in some cases taken a more conventional view, restricting themselves to *bis*(cyclopentadienyl) complexes.

There is also some divergence of opinion between authors regarding the discussion of applications. Contrary to expectations, this discussion is not confined to Volume 2. Several chapters in Volume 1 have extensive sections dealing with the topic, although others have none.

Chapter 1 by Jutzi and Burford reviews the chemistry of main group element compounds with π-bound cyclopentadienyl rings, much of it emanating from Prof. Jutzi's own laboratory. In Chapter 2 Edelmann covers the synthesis and reactivity of "lanthanocenes", pre-empting in some cases Chirik and Bercaw's discussion of Group 3 metallocenes in Chapter 3.

Chapters 4 and 5 respectively deal with titanocenes (Beckhaus) and zirconocenes (Negishi and Montchamp). Prof. Beckhaus is unique in this book in including a section dealing with spectroscopic data, which practitioners in the field may find particularly useful. Treatment of chiral titanocene and zirconocene dichlorides is deferred to Chapter 8 (Haltermann) which is concerned solely with the synthesis of such compounds.

The metallocenes of the elements of groups 5 and 6 are covered in Chapter 6. A huge number of compounds of this type is known and Prof. Royo and Dr. Ryan have devised a sensible system of classification in order to divide up the available material. Chapter 7 (Okuda and Eberle) deals with half-sandwich complexes which may be considered as metallocene analogues, a topic which could perhaps have been treated more broadly and formed the basis of a separate volume.

In Chapter 9 Prof. Janiak discusses the use of metallocene catalysts for olefin polymerisation. Chapters 10 (Hoveyda and Morken) and 11 (Togni) deal respectively with the applications of chiral titanocenes and zirconocenes, and of chiral ferrocenyl ligands in asymmetric synthesis. Metallocene-based polymers are considered in Chapter 12 (Peckham, Gomez-Elipe and Manners). There is a comprehensive index to all chapters at the end of Volume 2.

There is bound to be some overlap between chapters in multi-authored books such as this. There are, however, instances where one feels a little more editorial control could have been exercised. Thus the decision to include separate chapters on lanthanocenes and on group 3 metallocenes has led to considerable repetition. Six chapters (no.'s 4, 5, 7-10) deal predominantly with the chemistry of the group 4 elements. This is a reflection of the current importance of these compounds, particularly in catalysis, but some duplication of material has inevitably resulted. For example, there is a section in Chapter 10 entitled "Asymmetric Propene Polymerisation", although this topic has already been covered in much greater detail in Chapter 9.

Surprisingly, given the title of the book, nowhere is there mention of the *bis*(cyclopentadienyl) compounds of manganese, cobalt and nickel. Whilst aspects of ferrocene chemistry are covered in Chapters 11 and 12, and in the companion monograph, a general discussion of the properties of the 'true' metallocenes is notably absent.

All the contributions to this book are of high quality, and will provide both the newcomer to the field, and the established expert, with a rich source of background information. There is an impressive number of references in each chapter, with over 2500 in total. These generally cover work published up to the end of 1996, with some dating from 1997.

The standard of the presentation is very good, and there are relatively few typographical errors. It is perhaps unfair to single out one example, but the caption to Scheme 4-11, which bears only partial relation to the reactions depicted above it, is clearly a mistake.

Although there have been other reviews of the organometallic literature, most obviously "Comprehensive Organometallic Chemistry I and II, G. Wilkinson, F.G.A.Stone and E.W.Abel, Ed.'s, Pergamon, 1982 and 1995, the selection of material presented here is generally both relevant and timely. Despite my reservations regarding the title, this book will be an enormous asset to any research group working with "metallocenes" in either academia or industry.

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