Books about Chemical Libraries for Chemical Libraries

Forword

The field of combinatorial chemistry has seen a collection of new books since the end of 1999 which should offer a suitable piece of literature for any interested reader (see box). As we have had the opportunity to review most of these works for *Angewandte Chemie*—some in earlier issues (●)[*] and some on the pages that follow (◆)—we want to give a comparative overview of the current literature and shed some light on the question: "Is there a suitable book on combinatorial chemistry for everyone?" In addition to the new publications, we want to include two older titles that are still highly recommendable for some readers.

Students will find the book by Daniel Obrecht and Jose M. Villalgordo a comprehensible and affordable introduction into the field of combinatorial chemistry. The essential principals of combinatorial chemistry are elucidated in great detail in the introductory chapters, and good sections on linkers and reactions on solid supports are also available.

Combinatorial chemists engaged in synthesis are especially addressed by the books from Barry A. Bunin and Florencio Zaragoza Dörwald. These books are combinatorial handbooks which present techniques, solid supports, linkers, and reactions in a highly ordered fashion, even supplying detailed experimental descriptions. When more detailed information is required, one can refer to the exhaustive list of citations. The "Zaragoza Dörwald" is far more up to date due to its later appearance (early 2000), although some readers may still prefer the "Bunin" because the content layout allows specific problems to be easily addressed and the cited literature is evaluated.

Günther Jung's book belongs to the all-round solutions of combinatorial literature as does Pierfausto Seneci's work; the "Bannwarth/Felder" represents a border-line case as it also belongs to the handbook category. All in all, the quality of these books is varied. "Jung" and "Bannwarth/Felder" are still recommendable because of their overviews on combinatorial solid-phase chemistry, linkers, multicomponent reactions, and high-throughput and solid-phase analytics, as well as the interesting views on chemosensors, RNA and DNA aptamers, and computer-aided library design, but "Seneci" has to be considered to be inferior to its competitors in practically all fields.

Finally, the book by Kevin Burgess does not fit in any of the above-mentioned categories. Here, specialized and very well written essays on topics like solid-phase synthesis of guanidines, palladium-catalyzed carbon–carbon bond formations, and the synthesis of benzofused heterocycles through S_NAr reactions on solid support are found. It is a highly recommendable book for every reader who is interested in one of the discussed topics. Here, we are looking forward to further editions of this series.

The exponential growth in the number of original publications within the field of combinatorial chemistry makes it difficult for book authors to keep up to date. We can only hope that new (revised) editions of the established (and good) works will be brought out at short intervals and that the new books will aim for the same high standards as some of their predecessors. Combinatorial chem-

- Solid-Phase Organic Synthesis
  Kevin Burgess (Ed.)
  John Wiley & Sons, Inc., New York 2000
  XIV + 277 pp., hardcover $ 69.95
  ISBN 0-471-31825-6
- ◆ Organic Synthesis on Solid Phase—Supports, Linkers, Reactions
  Florencio Zaragoza Dörwald
  Wiley-VCH, Weinheim 2000
  XIX + 474 pp., hardcover 268.00 DM
  ISBN 3-527-29950-5
- Combinatorial Chemistry—Synthesis, Analysis, Screening
  Günther Jung (Ed.)
  Wiley-VCH, Weinheim 1999
  XXXII + 602 pp., hardcover 268.00 DM
  ISBN 3-527-29869-X
- ◆ Solid-Phase Synthesis and Combinatorial Technologies
  Pierfausto Seneci
  Wiley-Interscience, New York 2000
  XII + 637 pp., hardcover £ 70.95
  ISBN 0-471-33195-3

  The Combinatorial Index
  Barry A. Bunin
  Academic Press, San Diego 1998
  XIV + 322 pp., hardcover $ 79.95
  ISBN 0-12-141340-3
- Solid-Supported Combinatorial and Parallel Synthesis of Small-Molecular-Weight Compound Libraries
  Daniel Obrecht, Jose M. Villalgordo
  Pergamon Press, Oxford 1998
  340 pp., softcover $ 49.50
  ISBN: 0-08-043258-1
- ◆ Combinatorial Chemistry—A Practical Approach
  Willi Bannwarth, Eduard Felder (Ed.)
  Wiley-VCH, Weinheim 2000
  XX + 430 pp., hardcover 268.00 DM
  ISBN 3-527-30186-0

  Combinatorial Chemistry—A Practical Approach
  Hicham Fenniri (Ed.)
  Oxford University Press, Oxford 2000
  XXXII + 476 pp., softcover £ 39.50, hardcover £ 75.00
  ISBN 0-19-963754-7, 0-19-963757-1
  This book was published too late to be included in this review. However, it will be separately reviewed in the near future.

[*] "Burgess": *Angew. Chem. Int. Ed.* **2000**, *39*, 4165; "Jung" *Angew. Chem. Int. Ed.* **2000**, *39*, 3145; "Villalgordo": *Angew. Chem. Int. Ed.* **2000**, *39*, 4165.

This section contains book reviews and a list of new books received by the editor. Book reviews are written by invitation from the editor. Suggestions for books to be reviewed and for book reviewers are welcome. Publishers should send brochures or (better) books to the Redaktion Angewandte Chemie, Postfach 101161, 69451 Weinheim, Germany. The editor reserves the right of selecting which books will be reviewed. Uninvited books not chosen for reviews will not be returned.

istry does not need to be reinvented all the time!

A comparison like this cannot be absolutely fair and some authors will surely disagree with the categorizations we have made. However, as few bookshops will be able to offer the whole range of books for a direct personal comparison, we hope with this preselection to have enabled interested readers to find the book that suits them best. The final decision remains, as always, a question of personal taste.

Organic Synthesis on Solid Phase—Supports, Linkers, Reactions. By *Florencio Zaragoza Dörwald.* Wiley-VCH, Weinheim 2000. XIX+474 pp., hardcover DM 268.00.—ISBN 3-527-29950-5

In recent years there have been several books on the topic of combinatorial chemistry and solid-supported organic chemistry published. However, the only guide for the scientist orientated towards preparative chemistry was "The Combinatorial Index" by Barry A. Bunin. Florencio Zaragoza Dörwald presents this book as an alternative. His work addresses the preparative chemist, who requires quick reference to transformations carried out on the solid phase. The first two chapters describe general techniques, analytical methods, and supports for solid-phase organic synthesis in a very concise way. In Chapter 3 the different anchoring groups are introduced, according to the type of compound cleaved. Conditions which lead to cleavage from the solid support are described later in the chapter. Although all yields and purities given in the following chapters are for the cleaved products, these compounds are only described in Chapter 3. In keeping with the period, Zaragoza Dörwald concentrates on the presentation of reactions on polystyrene and polyethylene glycol based supports.

The following 14 chapters describe different transformations on the resin and the synthesis of different types of products. A speciality of this book is the 14 experimental procedures. Attributed by a grey background, they are easily recognised and give short instructions that are sufficient for a synthesis on solid support without consulting the original literature. Every chapter starts with an introduction of the discussed reaction. Afterwards, the different routes of the transformations are explained. Starting materials, products and, in a short form, the reaction conditions are introduced in tables. An exception to this procedure is the last chapter, which describes the preparation of peptides, oligosaccharides, and other oligomeric compounds. Here general strategies which lead to the target compounds are given. Treating these methods in the form of tables, as in the preceding chapters, would probably have been beyond the scope of this work. The literature indexes, which are given for every chapter, are comprehensive and very up to date. Articles published until mid 1999 are taken into account, an extremely pleasing situation! Further on, other related publications are cited, so the reader is able to find further leading literature. The actuality of the cited publications is a possible explanation for the quality of the pictures on page 385, which is strongly reminiscent of a fax copy.

With this work Florencio Zaragoza Dörwald provides a very well presented reference book, which also contains the newer developments in the chemistry of solid-supported organic synthesis. The already-mentioned experimental procedures are, due to their own index, easy to find and they are helpful in carrying out standard reactions. This book is not very well suited as a textbook—the descriptive passages only give a short overview on the content of the tables. This is completely redeemed by the extensive literature references. As a reference work, this book should not be missing from any laboratory where research in the field of solid-phase chemistry occurs.

M.L., S.B.

Solid-Phase Synthesis and Combinatorial Technologies. By *Pierfausto Seneci.* Wiley Interscience, New York 2000. XII+637 pp., hardcover £70.95—ISBN 0-471-33195-3

With this book Pierfausto Seneci presents an additional work belonging to those classed as "comprehensive". In over 620 pages covering 11 chapters, all thinkable fields of combinatorial chemistry are discussed. These range from the principles of solid-supported synthesis and the synthesis of oligomeric and non-oligomeric organic molecules, through library design and library synthesis, to the application of combinatorial methods in materials science and polymer chemistry.

Although the first chapter (solid phases, linkers, reaction monitoring on solid support) is still appropriate for beginners in this field, it is far from being comprehensive or even up to date. In the third chapter the author's origin in pharmaceutical research becomes obvious (he is Associate Director of Chemistry at the GlaxoWellcome Medicines Research Center in Verona). He tries, in this chapter, to point out the development of substance libraries (target, retrosynthesis, and validation of the synthetic route in solution as well as on the solid phase) by giving examples of libraries of biologically active compounds. Thereby, he puts a lot of emphasis on complex and diverse structures whereas the chemical methodology is more or less neglected. Some of the schemes contain a few reaction details and structures of reactants, which are called monomers (for reasons that we do not fully understand), whereas others represent planned reaction sequences without any comments on the reaction details. In a lot of cases these two types of schemes are presented close to one another on the same page and confuse the reader more than they help him to understand the intentions of the author. The integration of the schemes into the text is also often misleading. In some schemes the errors pile up to such an extent (for example, Figure 3.28) that further reading is made difficult. Chapter 4 deals with the principles of combinatorial chemistry and contains, besides a short combinatorial glossary, a historical overview of the development of combinatorial chemistry and a compilation of compound libraries that do not help the reader a lot in this form. The recycling of graphics which are found, in a similar or even in the exact form, throughout the following chapters also begins here (for example, Figure 4.1 reappears a couple of times in Chapter 5). Overall, we gathered the impression that the introductions to the different chapters are repeated in a slightly changed form.

Seneci has a habit of finding abbreviations for every technical term he uses, whether necessary or not. To abbreviate Solid Phase as SP or Solid-Phase Synthesis as SPS may still be common and

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reasonable. To use CC instead of Cyclative Cleavage, TL for Traceless Linker, or SC for Safety-Catch Linker is, at least in our eyes, exaggerated and leads only to hardly readable passages or subtitles like "Examples for CC on SP". As in most books on combinatorial chemistry published recently, the author has to be criticized for the quality of the graphical presentation. Not only does Seneci use the least attractive symbols for solid supports so far found in the literature, but the uniformity and size of the schemes is not maintained in the different chapters. In edited books containing attributions from different authors this may still be understandable (although an editor can still take care to provide an adequate presentation, as K. Burgess has in the case of "Solid-Phase Organic Synthesis"), but a single author should be able to stick to a continuous style throughout. This has just recently been shown in "Organic Synthesis on Solid Phase–Supports, Linkers, Reactions" by F. Zaragoza Dörwald.

Seneci wants to address the advanced (combinatorial) chemist as well as the student. The advanced chemist will sooner or later miss a detailed and comprehensive collection of linkers and reactions, whereas the student will perhaps be better served by a shorter and more easily understandable book (for example, one lacking chapters about library design or biosynthetic combinatorial libraries). All in all, Seneci has delivered a fairly comprehensive (or at least voluminous) book which will, however, probably have difficulties finding a suitable readership due to its very strong competitors.

S.D., S.B.

Combinatorial Chemistry—A Practical Approach. Edited by *Willi Bannwarth* and *Eduard Felder*. Volume 9 in the series *Methods and Principles in Medicinal Chemistry*, edited by R. Mannhold, H. Kubinyi, H. Timmermann. Wiley-VCH, Weinheim 2000. XX+430 pp., hardcover DM 268.00—ISBN 3-527-30186-0

The ninth volume in the series "Methods and Principles in Medicinal Chemistry" deals with combinatorial chemistry and takes into account the importance of this field in medicinal chemistry. The eleven authors (W. Bannwarth, W. Brill, A. Dominik, E. Felder, B. Hinzen, T. Krämer, A. Marzinzik, J. Pernerstorfer, A. Scannell-Lansky, S. Weinbrenner, and C. Zechel) for the eight chapters are mainly experts in the field of pharmaceutical chemistry.

The first three chapters deal with the three modern topics in the field of organic combinatorial chemistry (liquid-phase and solid-supported combinatorial chemistry, and the usage of polymer-bound reagents) and take up nearly one third of the book. The chapter on liquid-phase combinatorial chemistry concentrates on multicomponent reactions and the separation of product mixtures. This includes the usage of scavenger resins. The following chapter, which with 160 pages is the most detailed, has its focus on solid-phase synthesis and deals with anchoring groups (40 pages), cyclization/cleavage strategies (20 pages), and C–C bond formation, as well as the synthesis of heterocycles. The third synthesis chapter is about polymer-bound reagents, which are of constantly increasing importance in high-throughput synthesis.

A short excursion into the field of decoding strategies follows a successful overview of automated synthesis and the available equipment. The readily available systems are introduced to the reader in clear tables. A "must" for the usage of combinatorial methods in medicinal chemistry is the computer-aided design of libraries, which is made clear to the reader on 50 pages. A list of reactions on solid supports from 1970 to 1998 is given in tables; the citation of over 600 (!) references completes this work.

A number of experimental details and some complete reaction data, which are mostly from the laboratories of the authors, are a constant theme running through this work. With the aid of these "recipes" the reconstruction of many transformations is defintely lightened. Hence, the authors and editors have come close to a "practical approach", as claimed in the title of the book. Noticeable while reading the book is the constantly good, but not completely uniform, graphical appearance. It enlightens the understanding of even complex matters. The index is well organized, but it is noticeable that in the third chapter the numbering differs by two pages and the cross-references within the chapter are incorrect. The literature included is, in most chapters, only from 1998 and earlier years, a drawback that is applicable to most of the works in this field. In some cases (Chapter 3), the reference to reactions carried out in the homogenous phase is so mixed up that it is not clear to the reader whether they are solid-phase reactions or not.

Altogether, in spite of the minor mistakes, it is a very good book and the medicinal chemist will appreciate this work as an enrichment and encouragement to his research.

M.L., S.B.

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Colour and Optical Properties of Materials. By *Richard J. D. Tilley*. John Wiley & Sons Ltd., Chichester 2000. xii+335 pp., hardcover £ 24.95.—ISBN 0-471-85198-1

Colors and dyes are of importance for many different scientific disciplines—whether physics, chemistry, biology, or materials science. While many books have been written about color effects and dyes, a generally comprehensive (and useful) book has not existed so far, with the exception of the one by H. Zollinger (*Color: A Multidisciplinary Approach*) which appeared very recently. The present book was written for direct use by students, and for a general course. Thus, the style and size of the chapters correspond to introductory lessons, even though very specialist topics are also touched upon. Much importance is given to the physical part. Six chapters with more than one third of the contents cover the general aspects of light and color, of light refraction and dispersion, of interactions between crystals and light, and of the formation of color in reflection, scattering, and diffraction. Five chapters follow which deal with different color aspects of chemical structures, and also include a number of biological effects. To name only a few topics, colors of street lights, some min-

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erals, molecules, charge transfer and luminescence effects, as well as colors of metals, semiconductors, and insulators are mentioned. Finally, three chapters deal with material science subjects, data transmission, displays, lasers, and holograms. All chapters are divided into short and understandable subchapters. Also, problems and exercises at the beginning and end of each chapter serve the function of a teaching book, as well as the articles and books given for "further reading". Solutions to several problems can only be found in the World Wide Web, as well as some additional comments referring to several subchapters.

A clear choice of topics and their presentation by the author is necessary if such a broad subject has to be presented within such a restricted space. In this book, mainly the physical processes are presented in greatest detail. The inorganic, and especially organic chemistry topics are mostly restricted to the generally interesting aspects, like natural dyes, color photography, or the color of red wine.

With such a wide range of topics, some mistakes are almost unavoidable. Some of them will be mentioned for the organic chemistry part in Chapter 8 as examples. Enough space for annotations and corrections by the reader will be available in any case, because the main text and figures fill less than 50% of each page. A wrong formula for the azoxy functionality is found on page 182, and the quite common cyano group in dyes is missing in the table. The CO_2H group on page 184 (left) has been drawn incorrectly, and a double bond is missing in the formula for chlorophyll on page 185. In the Ni and Cu complexes shown four equal bonds have been drawn to the ligands, but two broken lines appear in the Mg and Fe complexes. Under "a" on page 200, a sextet resonance structure with a positively charged nitrogen was chosen for the *p*-phenylenediamine derivative, which is not quite suitable for the following substitution. On the next page, one symbol for the nitrogen of Cyan is missing in "c", which wouldn't be formed without an additional oxidation step anyway. On page 201, NH protons are missing for reaction "d", as well as the additional oxidation.

Nevertheless, the book offers an interdisciplinary presentation of color in a stimulating fashion. It would support a course which combines the color aspects of different subjects—which still (how long?) does not exist, at least in the places known by the reviewer. The future will show whether the book will be successful with the current rigid separation of lectures into different special topics. Until then—I recommend the purchase of this book to everyone interested in color.

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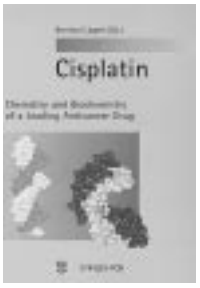
Cisplatin. Chemistry and Biochemistry of a Leading Anticancer Drug. By *Bernhard Lippert.* WILEY-VCH, Weinheim 2000. viii+563 pp., hardcover DM 298.00.—ISBN 3-906390-20-9

If there was a gold medal for the "most bioinorganic" compound ever, it should surely be awarded to Cisplatin. The compound $[PtCl_2(NH_3)_2]$ has been known since 1844. Around the turn of this century, it served Alfred Werner as proof for his theory on coordination compounds. In 1969, Rosenberg published his seminal findings that Pt compounds may inhibit the growth of tumors. Only a few years went by between the first clinical trials in 1972 and worldwide approval of *cis*-$[PtCl_2(NH_3)_2]$—called cisplatin—and this simple compound remains one of the most important anticancer drugs to the present day. It has saved the lives of thousands of patients, especially in the case of testicular cancer. Estimated annual sales are around 500 Mio. US$, and there are thousands of scientific papers dealing with cisplatin.



As editor of the book "Cisplatin—Chemistry and Biochemistry of a Leading Anticancer Drug", Lippert has undertaken the formidable task of summarizing this huge area of research. Thanks to the efforts of the editor and his authors, the book presents an excellent and up-to-date overview of research on cisplatin and related antitumor drugs 30 years after the original discovery of Rosenberg. It comprises 22 chapters in six parts, which are all written by leading experts in the field. After an introductory chapter by Rosenberg and a comprehensive overview on clinical applications of Pt antitumor drugs by O'Dwyer, the remaining four parts describe the biochemistry of cisplatin (four chapters), interactions of Pt compounds with biomolecules (seven chapters), inorganic chemistry revived or initiated by cisplatin (four chapters), and new developments (four chapters). Even if some of the articles recently appeared in a similar form (e.g. in a thematic issue of *Chem. Rev.* on Medicinal Inorganic Chemistry in 1999), this book is much more than a collection of review articles. A common layout with unified citations of all articles adds to the favorable overall impression as does cross-references between the articles. Color figures contribute to the high technical quality. All articles are of high quality and up-to-date. In most cases the literature is indeed covered up to 1998.

The scientific quality of this book is without doubt, but some thoughts on the topic in general came to my mind upon reading this book. Hundreds of publications deal with the chemistry and biochemistry of cisplatin (parts 3 and 4 cite over 1100 papers, although this number includes repeated citations) and this equals numerous doctoral theses and postdoc years. The reasoning behind this massive (and expensive!) research effort states that if the mechanism of action of cisplatin is understood on the molecular level it will be possible to design more powerful and more specific, in short: better, drugs in a rational way. After reading this book, one realizes that this aim has not been achieved. Moreover, one may be doubtful as to whether it may be achieved at all, at least in the foreseeable future. This book documents in impressive detail how well we understand the interaction of cisplatin with DNA and many other biomolecules in the human body. Still it remains a mystery why some tumors are amendable to cisplatin treatment while others are not. Even on a molecular level, it is

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not known whether all lesions in DNA that are set by cisplatin are equally dangerous or whether just one single, lethal type induces apoptosis. All experiments show that cisplatin and carboplatin, the second Pt anticancer drug in worldwide use, finally lead to exactly the same DNA damage, despite quite different pharmacokinetics. Why is it then, that cisplatin is still more active clinically in a number of cases? And finally, what about the most promising third generation Pt drugs, which are described by Farrell and Kelland in the final part of this book; which specific insights from cisplatin research lead to their development? The answer is deeply disappointing. The development of orally active Pt drugs follows general pharmacodynamic rules more than anything else and a promising candidate has been identified by biological screening of a compound library. The same holds for new oligonuclear Pt drugs. It is still trial-and-error, although at a very high level.

It should be mentioned, however, that this situation is little different from the development of other anticancer drugs, e.g. taxol. Moreover, although research in this area did - unfortunately - not lead to the discovery of new drugs, the close collaboration of inorganic chemists, medical doctors, pharmacologists, biologists, and molecular biologists stimulated research in many other unrelated areas, such as toxicology of heavy metals and the role of metal ions in gene regulation. Research on cisplatin also induced methodological advances. This is nicely illustrated in the chapters by Lippard and on NMR investigations by Marzilli and Sadler. This book does not present a guide on "how to build the best anticancer drug ever" and there is little hope of paying for the price of this book from patent loyalities. In almost all other respects, however, it is an excellent investment and a great pleasure to read. One needs to spend a very long time in the library and copy a great number of original papers to get a similarly outstanding overview of a topical area of chemistry!

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Chemistry of Fireworks. By *Michael S. Russell*. Royal Society of Chemistry, Cambridge 2000. xviii+118 pp., paperback £ 18.95.—ISBN 0-854598-8

This book, written by a chemist and enthusiastic amateur pyrotechnician, not only describes the chemical and physical basis of pyrotechnics but also gives the reader a more detailed understanding of the construction, function, and mechanism of fireworks. It also contains advice about the safe use of fireworks, and explains the legal requirements (at least as they exist in Great Britain) concerning their manufacture and use. Within that framework the author has written a concise and easily understandable survey of the main aspects of modern fireworks, which makes entertaining reading.

The book begins with a brief summary of the history, mainly in the British context, of the discovery and development of the so-called black powder (gunpowder). There is interesting historical background information about its English discoverer, the monk Roger Bacon, and about Guy Fawkes, the medieval terrorist, who in 1605 attempted to blow up the Houses of Parliament using 36 barrels of black powder, an event now commemorated every year on "Guy Fawkes Night".

Black powder, being nowadays still the main ingredient of fireworks, is the subject of a whole chapter devoted to the relevant chemistry, the kinetics and thermodynamics of the reaction, and thermal analysis data, treating selected aspects in detail. This is followed by chapters on the construction, function, and mode of action of fireworks in various forms: rockets, bombs, fountains (or "waterfalls"), fairy candles, sparklers giving "golden rain", firecrackers, jumping jacks, Roman candles, and Catherine wheels. Here the author explains, in a simplified and easily understandable way, the principles of loading in the black powder to generate impulses for movement or shooting out projectiles. He explains the laws governing the action of a rocket, and the height to which a bomb can be shot into the air using a given quantity of charge. Interspersed with the descriptions of applications are technical details concerning the generation of sparks and the mechanism of the burn-up of metal particles from fireworks, sound production, estimating the loudness of firecrackers, and the basic principles of generating colored light from pyrotechnic stars. This strongly application-orientated section of the book ends with descriptions of ignition devices (e.g., using covered stops), jet nozzles, and supporting structures.

The chapters on pyrotechnic devices for generating bangs, whistles, and smoke are again chemistry-orientated, but are regrettably rather short. In particular, the chapter on whistle-generating devices does not cover intermittent burning, nor does it include recent developments that have occurred in this and other areas of pyrotechnics during the last 20 years. However, that does not detract from the very positive impression left after reading this book.

As explained in the preface, the book does not claim to cover the subject exhaustively. However, it achieves its aim of giving an easily understandable introduction to the chemical and physical fundamentals of the art of fireworks. It succeeds not so much through giving a catalogue of pyrotechnic formulations and recipes as through its explanations of the physical and chemical modes of action of the best known types of fireworks.

The reader who wishes to gain an insight into the technology of fireworks or a deeper understanding of their construction and function will find much valuble material here. Moreover, the book is written in a pleasing, easily understandable, conversational style in straightforward English. A glossary of the most important technical terms is provided for nonspecialists.

Experts in the subject and those working in the fireworks industry will already be familiar with much of the book's content. On the other hand, laypeople, students, engineers, and scientists with an interest in fireworks will find this book to be a useful source of information which makes absorbing reading.

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