book content, wherever and whenever needed, it is hyperlinked through easy-to-use browsing and search functions, is searchable on book chapter level, and is integrated with Springer Online Journals.

The 3rd edition of *Multiple Bonds between Metal Atoms* deals with one of the most active fields of inorganic chemistry, which comprises all but two of the d-block transition metals in Groups 5–10. It presents an extensive, critical review and discussion of preparations, reactions, bonding, and physical properties of more than 4000 compounds with metal–metal bonds of orders 0.5 to 4, and about 2500 references. I heartily recommend it to inorganic and materials chemists, and to all scientists concerned with the synthesis, spectroscopy, and structures of transition-metal compounds. It also belongs in academic, industrial, and government research libraries.

George B. Kauffman
California State University
Fresno, CA (USA)

Sequence-specific DNA Binding Agents

Edited by *Michael Waring*. Royal Society of Chemistry, Cambridge 2006. 258 pp., hardcover £79.95.—ISBN 978-0-85404-370-5

Most drugs are now designed to target specific proteins, and that principle will continue in the future. However, another major class of biological molecules, nucleic acids, has also attracted considerable attention as a source of potential targets for drugs. Of two important subclasses of nucleic acids, DNA and RNA, the latter looks much more attractive as a candidate for sequence-specific targeting, since it exists in the cell predominantly in single-stranded form. As a result, individual nucleobases are accessible for interaction with drugs. In contrast, DNA exists in the cell predominantly in duplex form, where bases are buried inside the double helix and are much less accessible for interaction with drugs. So the sequence-specific targeting of DNA, which is the theme of this book, presents the greatest challenge from the viewpoint of drug design. In recent years it has become evident that DNA-binding drugs are extremely important for medicine, as the mechanisms of action of chemotherapeutic drugs that were discovered by empirical means were progressively unraveled. DNA is now seen as the primary target for the most potent chemotherapeutic drugs. Therefore, the subject of this book is of great significance.

There is an enormous variety in the specific mechanisms of action of DNA-binding agents, and many of them operate not by themselves but in conjunction with various proteins working on DNA in the cell. Consequently, in many cases the description of the mechanism of action of the drug presents a fascinating story that involves the triangle DNA/drug/protein. Some of these stories are narrated in this volume. Of course, not all the stories on the subject are told (nobody can embrace the unembraceable), and not all the stories in the book are equally compelling, but the fact is that I found it difficult to put the book down.

The chapters that I found most entertaining and inspiring were those in which the authors not only tell the scientific story behind the discovery but also narrate, in a very vivid style, the history of the discovery. This is especially true for two adjacent chapters, one by S. Neidle and the other by D. Sun and H. Hurley. These are devoted to a new class of potential anticancer drugs, which bind specifically to G-quadruplexes. The cell targets for these drugs are single-stranded telomeric tails, which are always present at the 3′ ends of chromosomal DNA. The repetitive sequence of these single-stranded tails (TTAGGG) is such that they can fold back on themselves to form a very unusual DNA structure known as a G-quadruplex. Telomeric tails serve as primers for the enzyme telomerase, which extends telomeric sequences in cancer cells, thus making them immortal. By stabilizing the form of the G-quadruplex, the G-quadruplex-binding drugs deny telomerase any contact with the primer, thus potentially preventing cancer cells from perpetual division. The G-quadruplex-specific drugs present a fascinating example of drugs that recognize an unusual DNA structure rather than a specific sequence. Of course, for DNA-binding drugs it is a special case based on the fact that the telomeric ends are in single-stranded form.

A more common situation, which is discussed in most other chapters in the volume, is that of sequence-specific binding to the regular duplex DNA, which adopts the canonical B form. Enormous efforts and real ingenuity have been exercised to develop numerous classes of drugs that recognize duplex DNA in a sequence-specific manner. Since, in the B form of DNA, the bases are buried within, one possibility for sequence-specific recognition is to "search" DNA from one of the two B-DNA grooves. This is exactly what triplex-forming oligonucleotides (TFOs) do, as described in the chapter by D. A. Rusling, T. Brown, and K. R. Fox. Unfortunately, the prospects for any therapeutic applications of TFOs are not bright, for a number of reasons, mainly because long homopurine tracts are needed for stable binding of TFO to DNA. Such long tracts are scarce in sensible genomic sequences.

With regard to possible applications as a drug, peptide nucleic acid (PNA) looks much more attractive, as P. E. Nielsen, a PNA pioneer, indicates in a short but very informative chapter. The neutrality of the PNA backbone results in the two short homopyrimidine PNA oligomers forming exceptionally stable complexes with the corresponding homopurine sequences in one of the two DNA strands. The complex is so stable that PNA oligomers exhibit a unique ability to form strand-displacement complexes with duplex DNA, in an exceedingly sequence-specific manner. As a result, PNA has proven to be a remarkable tool for targeting duplex DNA.

Several chapters in the volume are devoted to more traditional small-molecule drugs that bind to DNA. Being small, these drugs can recognize only very short sequences, and therefore they cannot be highly selective. That does not make them less important for medical applications. On the contrary, these are the drugs that are widely used in clinical practice, mostly in cancer chemotherapy. Two chapters by C. Marchand and Y. Pommier and by N. Dias and C. Bailly narrate a fascinating tale about how these drugs interfere with topoisomerase I activity in the cell.

Biophysical methods play a crucial role in the study of DNA–drug interactions, and therefore it is appropriate that several chapters of the book are devoted to them. L. M. Wilhelmsson, P. Lincoln, and B. Norden discuss the kinetic aspects of DNA–drug interaction. F. Gago tells a personal story about his involvement in computer simulations of DNA–drug interactions using molecular dynamics. J. B. Chairs and X. Chi revisit, from a new perspective, an old question of the influence of drug binding on DNA melting profiles.

One chapter, by A. Serganov and D. J. Patel, describes RNA–drug interactions. Although the chapter is very interesting, it has a lonely position in this book, since targeting single-stranded RNA is a huge separate subject (especially in the light of siRNAs and related issues), which is beyond the scope of the volume.

In conclusion, many researchers in both industry and academia will find the volume extremely useful and inspiring. It achieves a very appropriate balance between breadth and depth, and also benefits from the personal touch of the authors.

Maxim Frank-Kamenetskii
Center for Advanced Biotechnology
Boston University (USA)

DOI: 10.1002/anie.200685487

