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BOOK REVIEWS

Metal Complex−DNA Interactions. Edited by Nick Hadjiliadis (University of Ioannina, Greece) and Einar Sletten (University of Bergen, Norway). John Wiley & Sons, Ltd.: Chichester. 2009. xx + 524 pp. $199.99. ISBN 978-1-4051-7629-3.

The study of metal complex−DNA interactions, referring mainly to DNA in its canonical B-form, continues to be an actively pursued but maturing area of research—a statement seemingly reflected by the contents of *Metal Complex−DNA Interactions*. Indeed, this volume brings together a very diverse array of topics related to metal−DNA interactions, from their DNA binding recognition to medical applications, that underscores the breadth of impact of the phenomena of metals and DNA but also indicates that the field has moved increasingly toward maturity. This is evidenced by the focused niche topics and scientifically worthy, but arguably incremental, advances addressed in some of the individual chapters. Also reflected, and a further indicator of the above, is the move of the field increasingly toward the study of metal interactions with noncanonical forms of DNA and the impact of metals on higher-order biological processes. Although canonical B-form DNA by far constitutes the main target of study in this volume, noncanonical DNA structures of current medicinal and biological interest—for example, G-quadruplex and telomere structures—are included among the topics covered as well as an overview of DNA repair mechanisms.

With regards to initial expectations, I found the title to belie somewhat the contents: "Metal *Ion*−DNA Interactions" or "*Metal*−DNA Interactions" would have been more descriptive, given the prominence of chapters emphasizing direct metal−DNA ligation in comparison to noncovalent interactions with coordinately saturated metal complexes. With this in mind, the book is organized into four main sections: "Basic Structural and Kinetic Aspects" (four chapters); "Medical Applications" (six chapters); "DNA Recognition: Nucleases and Sensors" (five chapters); and "Toxicological Aspects" (three chapters). There is a range in the quality, timeliness, and significance of the individual chapters included under these headings.

The opening section initiates the reader with two chapters that include theoretical studies of the fundamental inner-sphere interactions of metal ions with B-form DNA that lead to binding site/nucleobase selectivity, NMR studies thereof, and thermodynamic considerations. It concludes with two similarly specialized chapters: one on alkali metal ion binding by G-quadruplex structures and the other on the engineering of unique supramolecular architectures through the exploitation of metal−nucleobase interactions—essentially a non-DNA chapter. This portion of the book, and indeed the entire volume, would have benefited greatly from a general overview of the topic of metals and DNA to set the stage for later chapters.

The second section brings together several chapters with the overarching theme of DNA platination and therapeutic DNA metalation—a mainstay pursuit in the field of metals and DNA. Chapters include discussions of dynamic interligand interactions within *cis*-platin analogues, DNA repair mechanisms, telomere targeting by platinum complexes, platinum group metals in the development of compounds for photodynamic therapies, platinum-modified oligonucleotides toward the development of antisense agents, and, finally, a brief review on Rh− and Sn−DNA interactions. The cohesiveness of this section was straightforward, and I found the chapters on DNA repair, telomere targeting, and agents for photodynamic therapy to be enlightening overviews likely to be useful to those less familiar with these particular areas.

Discussions of reversible interactions of coordinately saturated metal complexes with DNA indeed are included in the third section. Three chapters explore the use of metal complexes for the purposes of probing fundamental recognition phenomena and DNA modification through metal-promoted phosphodiester hydrolysis. In addition, this part concludes with two chapters outlining, respectively, the generation of metal-based DNAzymes and DNA processing metalloenzymes. It was surprising to find the latter chapter in the volume, but it is easily rationalized based on the subtheme of DNA hydrolysis. Overall, these chapters were of good quality as stand-alone entities.

In the final section, "Toxicological Aspects", the chemistry of mercury, chromium, and arsenic were seemingly "cherry-picked" for inclusion. Although the chapter devoted to chromium really "hit the mark" with regard to examining the toxicity of this metal in its various oxidation states and the ramifications of their interactions with DNA, the chapter devoted to mercury emphasized little toxicology and was mostly an exposition on structural aspects of this particular metal−DNA interaction and the history of their elucidation. Finally, the chapter on arsenic dealt little with DNA beyond the induction of genetic damage by arsenic metabolites through indirect means, such as interference with DNA repair processes and increased oxidative stress. This portion of the book seemed incomplete with respect to the stated topic and was missing, for example, Ni−DNA interactions, among others.

Overall, *Metal Complex−DNA Interactions* attempts to bring together a variety of topics related to metals and DNA under one title—a daunting task when pursuing a cohesive volume but, as noted earlier, somewhat reflective of the ever-broadening and maturing nature of the field itself. As mentioned previously, the book as a whole would have benefited from introductory chapters for each section that could have explored the topic in general and explicitly related the contents of each specialized chapter to the central theme. Here also, I would be remiss not to mention that the volume would have benefited from careful copyediting as I noted a number of, at times, obvious typographical errors within the main text and references. Given the variety of topics and the spread of chapters found within the sections, the contents should be viewed as if they were proceedings of a symposium on metals and DNA, thereby resulting in a collection of distinctly individual chapters with their own merits. Indeed, the individual chapters predominantly reflect the contributions to the field made by the laboratories of the individual author(s) as opposed to broad reviews of the titled areas.

10.1021/ja907261x CCC: $40.75

Laudably, the editors selected a slate of authors from across the globe who provide a diverse perspective of the field. Thus, given the wide array of topics and the highly specialized content of most chapters, this book will mainly impact researchers already specialized within the fields covered. Individuals considering its purchase should peruse the Table of Contents, freely available on the Web, to determine the relevance to their needs and expectations. A library acquisition is recommended; however, this collection could also be useful as a resource for any graduate-level special topics course in the general area of metals and DNA.

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JA907261X

10.1021/ja907261x

Quinone Methides. Wiley Series of Reactive Intermediates in Chemistry and Biology, Volume 1. Edited by Steven E. Rokita (University of Maryland, College Park). John Wiley & Sons, Inc.: Hoboken, NJ.2009. xviii + 432 pp. $125. ISBN 978-0-470-19224-5.

This book represents the inaugural volume in the "Wiley Series on Reactive Intermediates in Chemistry and Biology". It is the first monograph entirely devoted to the discussion of the generation, properties, and biological function of *ortho*- and *para*-quinone methides (QMs). In fact, the only other book that has some information on the chemistry of quinone methides is the 30-year-old volume *Houben-Weyl Methods of Organic Chemistry, Volume 7, Part 3B*. The present volume consists of 12 chapters summarizing the progress of current research in this area. The chapters are well written and include concise abstracts, overviews of the latest findings in the field, discussions of emerging applications, and comprehensive lists of references. Since the focus of the series is on reactive intermediates, the mechanisms of reactions involving QMs and the reactivity of these species, rather than synthetic methods utilizing their reactivity, are discussed.

The first part of the book deals with the formation, properties, and reactivity of QMs. Photochemical methods, discussed by Lukeman in the opening chapter, enable efficient and "reagentless" generation of QMs under mild conditions. QMs are most commonly prepared by the elimination of a benzylic substituent from *ortho*- or *para*-hydroxybenzyl precursors. Photochemical methods provide an opportunity to employ thermally stable QM precursors that possess poor leaving groups, such as the hydroxy or alkoxy group. Laser flash photolysis of appropriate precursors produces substantial concentrations of targeted QMs and allows for the spectroscopic detection and direct measurements of the reactivity of these species. The second chapter is focused on the computational analysis and modeling of the reactivity of QMs. Freccero and Doria show that DFT methods can reliably predict properties and the reactivity of these species both in the gas phase and in solution.

Most QMs are short-lived intermediates produced and immediately consumed in the course of various chemical and biological processes, although complexation to low-valent transition metal centers allows for stabilization and modification of the reactivity of QMs. The chemistry of such complexes, including release of QMs and potential synthetic applications, are discussed in Chapter 3. Chapter 4 is devoted to the discussion of synthetic methods that utilize low-temperature generation of *ortho*-QMs and similar intermediates.

The second part of the book covers several important applications of QM chemistry, as well as mechanistic studies of biochemical processes, which are believed to proceed via the formation of QMs. Thus, Erez and Shabat describe construction of self-immolative dendritic molecules. The spontaneous disassembly of these dendrimers is based on the rearrangement of quinone or azaquinone methides, and the cascade release of several drug molecules after an enzymatic deprotection of a phenolic hydroxy group of a substrate is enabled by this strategy. In Chapter 6, Rosenau and Böhmdorfer discuss the mechanism of the antioxidative action of vitamin E. It has been recently shown that *ortho*-QM intermediates are formed during the oxidation of tocopherol. The authors then analyze the regio- and chemoselectivity of the process, as well as subsequent reactions of *ortho*-QMs.

The formation and reactions of QMs are also believed to be responsible for the cytotoxicity of several important classes of antibiotics belonging to the mitomycin, anthracycline, and kinamycin families. However, the reactivity of QMs generated in the dark, for example, by a two-electron reduction of quinones followed by elimination of the leaving group, is more complicated than photochemical studies owing to relatively slow generation of the target species. Fortunately, mechanisms of these reactions still can be investigated using global spectral kinetic analysis and targeted ^{13}C-labeling of quinonide positions. Practical applications of these techniques to the studies of the formation and reactions of reductively generated QMs are discussed by Skibo in Chapter 7.

In the following chapter, Zhou covers the biochemical function, reactions, and total syntheses of many naturally occurring *para*-QMs. Chapter 9 returns the reader's attention to the mode of action of QM-forming antibiotics. In this chapter, Rokita reviews reversible alkylation of DNA by *ortho*-QMs. Detailed discussion of the mechanism of the reaction and analysis of the kinetics and substituent effects on the efficiency as well as sequence-selectivity of alkylation paves the way for the design of improved DNA-targeting antibiotics. Next, the role of QMs in the toxicity of *ortho*- and *para*-alkyl phenols is reviewed. Thus butylated hydroxytoluene, a common antioxidant; eugenol, a component of clove oil; and tamoxifen, a pharmaceutically useful antagonist of the estrogen receptor, are hydroxylated and/or oxidized by the ubiquitous enzyme P450 to generate QMs.

The penultimate article in the book focuses on *para*-QM-based inhibitors of serine proteases and serine-β-lactamases. The design of these suicide inhibitors is based on the enzymatic release of aromatic hydroxy or amino groups, which then triggers the formation of a QM. The latter reacts with histidine residue located in the active site of the substrate and permanently disables the enzyme. The final chapter is a review of the role of QMs in the biosynthesis of lignin and lignan, as well as in the degradation of these biopolymers. The authors analyze the mechanisms of these processes and discuss the implications of QM chemistry on the use of lignocellulosic biomass as an industrial feedstock.

In summary, this book should serve as a valuable source of information on the properties and chemistry of various quinone methides, as the data on QMs are scattered throughout numerous publications and rather difficult to locate. The subject index at the end of the book is especially helpful. I believe that many chemists, both in academia and in industry, will find this volume

to be a useful addition to their libraries. I would also recommend this book for institutional library collections, where it will serve as a valuable reference source.

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JA907034G

10.1021/ja907034g

Metal Ions in Life Sciences, Volume 5: Metallothionein and Related Chelators. Edited by Astrid Sigel, Helmut Sigel (University of Basel, Switzerland), and Roland K. O. Sigel (University of Zürich, Switzerland). Royal Society of Chemistry: Cambridge. 2009. xxx + 514 pp. $299. ISBN 978-1-84755-899-2.

The series of volumes edited by the Sigels, originally *Metal Ions in Biological Systems* and now *Metal Ions in Life Sciences*, has provided useful thematic collections of articles for 36 years. The latest, however, is only the second of these 50 volumes devoted primarily to a single protein—it is no surprise that the first was cytochrome P-450. Since its discovery over 60 years ago, metallothionein (MT) has been studied extensively and has been the subject of previous books, several from international meetings on this small Cys-rich metal-sequestering protein, although none in the past decade. This volume consists of 15 well-referenced chapters by individuals who have a long history with MT (Nordberg, Vašák, Schaffner, Weser, Petering, Waalkes) as well as newer investigators (Blindauer, Freisinger, Atrain, Stürzenbaum, Vergani) and an extensive index. It highlights recent results on unique MTs (some involving His coordination) from lower organisms, including those from bacteria, insects, terrestrial and aquatic invertebrates, and plants. Authoritative chapters also summarize our current understanding of the control of MT gene expression, the neuronal isoform MT-3 implicated in neurodegenerative disease, and the role(s) of MT in metal toxicity and carcinogenesis. Missing, but available in recent issues of the *J. Am. Chem. Soc.*, are new results on MT coordination of As^{3+} and Zn^{2+} by Stillman and Maret, respectively. This volume maintains the high quality of this series and is a timely resource for investigations of metal homeostasis and detoxification, in particular those addressing evolutionary questions and those considering organisms for environmental monitoring of toxic metals.

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JA907058Z

10.1021/ja907058z