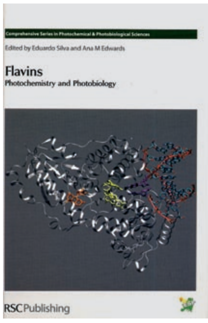
Flavins—Photochemistry and Photobiology



Edited by *Eduardo Silva* and *Ana M. Edwards*. Royal Society of Chemistry, Cambridge 2006. 328 pp., hardcover £ 169.95.—ISBN 978-0-85404-331-4

This compilation of articles covers a very active field of research, which has developed rapidly in the last few years, following the discovery of several biological photosensors that have flavins as chromophores. These new findings have fundamentally changed the paradigms in this scientific area, since the flavin chromophore, in contrast to the other known photosensors (phytochromes, sensory rhodopsins, and photoactive yellow protein, PYP), is attached non-covalently to the relevant apoprotein, and does not undergo a *cis–trans* isomerization upon photoexcitation. Also, very surprisingly, it is found that in several of the new photosensors the excited flavin reacts from the triplet state. This is the first known case of a chromophore triplet state participating in a biologically vital function.

The authors of the articles in this compilation include (in Chapters 8–11) several of the actual discoverers, who have made important contributions to the elucidation of the photoinduced mechanism in these photosensors, and are therefore able to describe, in a very detailed and interesting way, the scientific developments in this area during the last decade. The first four chapters deal with the spectroscopy and photochemistry of flavins in solution, then Chapter 5 describes the use of excited riboflavin as an antiviral and antibacterial agent. Chapter 6 discusses the phototoxicity of flavins, and Chapter 7 the possible role of flavins in photoinduced damage to the eye lens.

The writing of the articles is very uneven. Several of the articles written by non-native English speakers should have received a more thorough editing. That applies, for example, to Chapters 1 and 2. In the initial chapters describing the properties of flavins in common solvents, it would have helped non-specialist readers if the numbering of the atoms in the flavin skeleton (as referred to in the text) had been shown in the structure schemes. Most of the articles could have been improved by including lists of abbreviations (especially Chapters 1 and 2). The IUPAC recommendations on nomenclature and symbols are not always followed (e.g., in Chapter 4 the rate constant k is not italicized, and in Table 1 of Chapter 5 the term optical density is used instead of absorbance). A serious nomenclature problem is the use of the mesomeric arrow instead of the equilibrium double arrow in the Scheme on page 4. In Chapter 3 not all symbols have been explained. The heading of Table 2 in Chapter 7 is not clear, and einstein (for mole of photons) should not be written with capital E. In addition, some of the chapters have a well-balanced final discussion, whereas in other chapters that is missing.

Because of the complexity of the spectral properties of flavins, Chapter 2 would have benefited by including spectra of flavins at different pH values. In this chapter, a critical discussion, beyond the mere listing, of the reactions of photoexcited flavins would have also been very useful. For example, how are the reaction rate constants of the excited flavins in their different protonation states related to the redox potential of the substrate?

Chapter 9, by Winslow Briggs, gives an excellent historical account and classification of the photosensors that contain flavins as chromophores. However, the chapter contains no figures with the known structures, nor any schemes with mechanisms—in fact, it contains no figures whatsoever. This makes reading the chapter a bit difficult, especially for readers new to the field. I enormously enjoyed reading this chapter (as well as others).

In spite of some criticisms, as discussed above, the book should be extremely useful for students starting in this fascinating and rapidly developing area of research, as well as for specialists who would like to have a comprehensive account of developments in this field in the last few years. To this end, the authors have also put together a very extensive and complete literature list at the end of each chapter. I recommend librarians to acquire this book for their scientific collections.

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Discrimination of Chiral Compounds Using NMR Spectroscopy

By *Thomas J. Wenzel*. John Wiley & Sons, Hoboken 2007. 576 pp., hardcover € 97.90.—ISBN 978-0-471-76352-9

During the last couple of decades, stereoselective synthesis of chiral compounds has been, and is, one of the major challenges in modern organic, pharmaceutical, and medicinal chemistry. A considerable number of Nobel Prize winners have worked in this field, and some are still engaged in it. Such syntheses need to be supported by suitable analytical methods; in other words, they are effective only if they are accompanied by quick and easy ways to determine enantiomeric purity and, where relevant, absolute configurations.

The most suitable methods are chromatography on chiral stationary phases and spectroscopy. Among the latter, only CD (circular dichroism) and VCD (vibrational circular dichroism) are intrinsically chiral and avoid the need for an additional chiral reference. Nevertheless, NMR spectroscopy—although it is an achiral method—is much more popular, not least because this technique is ubiquitous and easily available in nearly all laboratories around the world.

Over many years, a great variety of chiral NMR auxiliaries have been invented and used. They create diastereomeric interactions between enantiomerically pure auxiliaries and the chiral substrates under study, leading to a doubling of NMR signals, which can be interpreted in terms of enantiomeric purities and absolute configurations.

The history of NMR spectroscopic techniques for chiral discrimination reaches back several decades. It began with the pioneering work of Raban and Mislow, published in 1965. In 1973, Mosher and Dale introduced MTPA (Mosher's acid), a "chiral derivatizing agent" (CDA), to be used for converting chiral alcohols or amines into diastereomeric esters or amides. The other innovative approach, in publications that began to appear in the late 1960s, was the use of Pirkle's alcohols and amines as solvent additives, which create diastereomeric adducts with chiral substrates without forming new covalent bonds. Thus, the concept of a "chiral solvating agent" (CSA) was born. This approach was superseded in the late 1970s by the introduction of chiral lanthanide shift reagents (CLSRs).

During the 1970s and 1980s, numerous reviews and monographs appeared describing these techniques and emphasizing their merits. Although more than 30 years old, the auxiliaries mentioned above are still popular, and are often employed for chiral recognition. However, it soon became apparent that although those methods are fine for studying alcohols, amines, carbonyls, carboxylic acids, and a few other compound classes, they do not cover other important ones—what about hydrocarbons, ethers, sulfur functionalities, and many, many others? Throughout the following years, researchers never stopped looking for new chiral auxiliaries to fill the gaps, and they are still searching. Most importantly for everyday practice, it turned out that using chiral NMR auxiliaries is often an empirical experiment with unpredictable results. Moreover, there is no all-rounder among them. Many substrates require specialized reagents to differentiate most effectively between enantiomers. There is now an immense body of literature describing various approaches and auxiliaries, covering a vast range of compound classes, functionalities, and experimental methods.

Although chiral discrimination by NMR auxiliaries is a mature field, new aspects and applications continue to be added, and that seems likely to go on for the foreseeable future. Thus, there has been a great need for a review that combines the essence of over 20 years of constant effort all over the world. Wenzel's book now fulfills that need. By presenting a comprehensive overview of the realm of CDAs and CSAs, the author fills a wide gap in the secondary literature.

To review this area and provide a structure for the extensive literature on the subject is not an easy task. Wenzel decided to organize his book in chapters, each of which is devoted to the crucial functionalities or structural peculiarities of the auxiliaries, not the substrates. This is a clear approach that is easy to comprehend, and serves the needs of the scientific community better than arranging chapters on the basis of substrate structures, which are sometimes multifunctional and therefore not easy to classify. Wenzel's approach demonstrates the range of applications of each auxiliary, and still allows the reader to find suitable reagents for a given substrate, especially since a comprehensive index of substrates is added at the end of the book.

An introductory chapter explains briefly the different kinds of auxiliaries (CDA, CSA, and others) as well as strategies for using them, and ends with an optimistic view of future developments. The main body of the book consists of chapters that deal with "Aryl-Containing Carboxylic Acids" (Chapter 2), "Other Carboxylic Acid-Based Reagents" (Chapter 3), "Hydroxyl- and Thiol-Containing Reagents" (Chapter 4), "Amine-Based Reagents" (Chapter 5), and "Miscellaneous Organic-Based Chiral Derivatizing and Solvating Agents" (Chapter 6). The advantageous NMR properties of some Main Group elements are compiled in Chapter 7, "Reagents Incorporating Phosphorus, Selenium, Boron, and Silicon Atoms". The final chapters deal with applications beyond classical organic chemistry: "Host Compounds as Chiral NMR Discriminating Agents" (Chapter 8), "Chiral Discrimination with Metal-Based Reagents" (Chapter 9), and "Chiral NMR Discrimination with Highly Ordered Systems" (Chapter 10).

The book contains nearly 1200 molecular structures and altogether 1668 references, covering the literature from as early as 1965 up to 2006. I cannot find a case of an important publication that is missing. If there is anything to criticize at all, one may mention the fact that it is not so easy to filter out recent work on the determination of absolute configurations by NMR spectroscopy. Although there is a great demand for effective methods in this area, and intensive efforts are continuing, progress is proving to be difficult. A review exists (cited as Reference [7]), but this is about 25 years old. Therefore, a corresponding keyword in the index or a separate chapter would have been helpful.

Tom Wenzel is a well-known researcher in the worldwide "chirality community", working intensively and successfully in the field covered by this book. In 2003, he published a review on that topic (*Chirality* **2003**, *15*, 256–270), and thus he is well qualified to prepare this huge and comprehensive—one might even say encyclopedic—compilation. Wenzel's book is not a textbook that can be read easily from cover to cover, or one that lecturers could use chapter by chapter in their seminars. Rather, it is a general reference book in its field for those who want to design effective experiments for chiral recognition of their compounds under investigation. In that sense, Wenzel's approach may be compared to that used by Eliel in his magnum opus on organic stereochemistry.

I strongly recommend that Wenzel's book should find a place in the library collection of every institution that deals with asymmetric synthesis, natural products, pharmaceutical chemistry, and stereochemistry in general, and in which NMR spectroscopy plays an active role in research. It should be ready to hand for every person working in any of those fields.

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