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**THE ASSIGNMENT
OF THE ABSOLUTE
CONFIGURATION BY
NMR USING CHIRAL
DERIVATIZING AGENTS**

A Practical Guide

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■ The Assignment of the Absolute Configuration
by NMR Using Chiral Derivatizing Agents

■ P R E F A C E

This textbook is written to help students and researchers to obtain the absolute configuration of organic compounds by nuclear magnetic resonance (NMR) using arylalkoxyacetic acids as chemical derivatizing agents (CDAs). Its origin can be traced to the postgrad courses I delivered in several universities over the years and to our investigations on this topic over a fifteen-year period. Now that we have decided to move to other fields of research, it is the perfect time to put together all our experience and knowledge in a way that makes the technique available for general users.

Our contribution to this field spanned from a study of the theoretical foundations to the development of new and more efficient auxiliary reagents, greatly expanding its range of applications. Those efforts helped to transform what at the beginning was almost no more than a scientific curiosity into a methodology that allows the determination of the absolute configuration of more than a dozen different classes of compounds by using ^1H and/or ^{13}C NMR. Nowadays, the assignment by NMR is the easiest and cheapest method in use, and it is available to all laboratories possessing basic NMR instrumentation.

The book is intended to be primarily practical but containing the minimal theoretical background necessary to understand the foundations and the results, and therefore, it is full of NMR spectra, experimental details, and examples of applications. All this material comes from our own laboratories and has been selected with teaching as the objective. Most of the figures were originally prepared and used as slides for projection and can be very useful for specialized courses. Naturally, any error in the book can only be our responsibility.

Finally, I would like to use these lines to acknowledge my coauthors, Emilio Quiñoá and José Manuel Seco, not just because this book would not exist without their contributions, but also because their presence in the laboratory and collaboration over the years has been to me a constant source of ideas, good work, and happy moments.

Santiago de Compostela, June 2014
Ricardo Riguera

■ INTRODUCTION

Over the years, the assignment of the absolute configuration of organic compounds [1–4] has been carried out using techniques such as circular dichroism (CD) [5–7] in solution, and X-ray diffraction [8–9] in the solid state. More recently, another two spectroscopic techniques have been introduced for the assignment in solution: vibrational circular dichroism (VCD) [10–12]—a technique currently available at a limited number of laboratories—and nuclear magnetic resonance (NMR) [13–15]. The latter, due to the extensive presence and use of NMR instrumentation in current research laboratories, can be considered to be of much more general applicability.

The use of NMR for the assignment of the absolute configuration of organic compounds is particularly useful in cases where the amount of the sample is limited, no monocrystals are available, or a rapid and inexpensive method is needed. In the last two decades, a great deal of effort has been invested in order to explain, to rationalize, and to extend the use of this methodology, which was initiated by Mosher and his colleagues in the 1960s [16–19]. Detailed descriptions, as well as other reviews of this topic, can be found in the literature [20–34].

The book shows in a direct way the foundations of the method, the general characteristics of arylalkoxyacetic acids as auxiliaries for chiral derivatizing agents (CDAs) [13–15], the classes of compounds whose absolute configuration can be assigned, and the scope and limitations of this technique. It is organized in such a way that Chapter 1 is devoted to the theoretical foundations, and Chapter 2 is dedicated to the practical aspects related to the NMR experiments, that is, the preparation of derivatives, reagent-supported resins, and auxiliary reagents. Chapters 3–5 discuss the application of this methodology for the assignment of configuration of different classes of organic compounds, including numerous examples and spectra. We have included in the final chapter, Chapter 6, a series of problems that can be used to test the knowledge attained by studying this book.

In order to facilitate its use for teaching, all the figures and spectra of this book in colour can be obtained from the publisher in a format appropriate for projection.

■ The Assignment of the Absolute Configuration
by NMR Using Chiral Derivatizing Agents

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