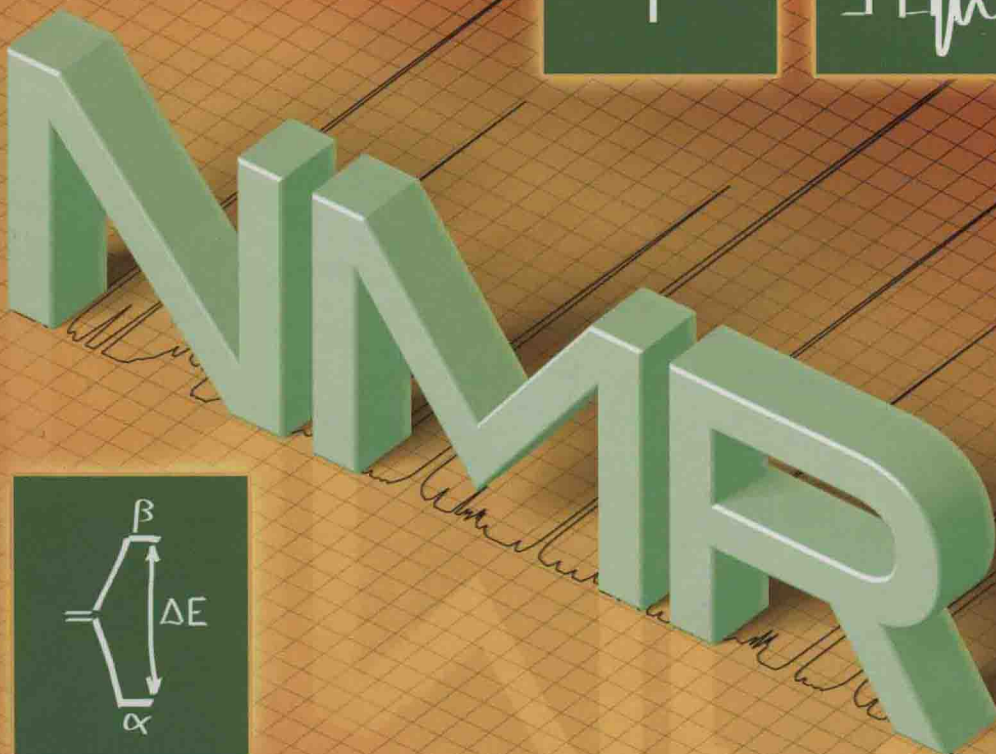
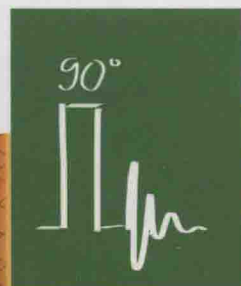
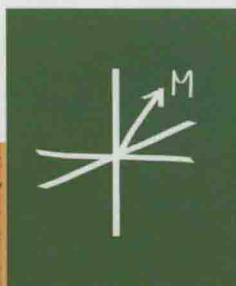


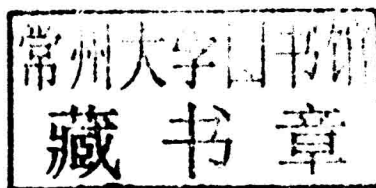
Oliver Zerbe and Simon Jurt

Applied NMR Spectroscopy for Chemists and Life Scientists



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WILEY-VCH
Verlag GmbH & Co. KGaA

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Library of Congress Card No.:

applied for

British Library Cataloguing-in-Publication Data:

A catalogue record for this book is available from the British Library.

Bibliographic information published by the Deutsche Nationalbibliothek

The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at <http://dnb.d-nb.de>.

© 2014 WILEY-VCH Verlag GmbH & Co. KGaA, Boschstr. 12, 69469 Weinheim, Germany

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Cover Design Formgeber, Mannheim

Typesetting le-tex publishing services GmbH, Leipzig, Germany

Printing and Binding betz-Druck GmbH, Darmstadt, Germany

Hardcover ISBN 978-3-527-32775-1

Softcover ISBN 978-3-527-32774-4

ePDF ISBN 978-3-527-67785-6

ePub ISBN 978-3-527-67783-2

Mobi ISBN 978-3-527-67784-9

Printed on acid-free paper

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Preface

NMR spectroscopy has developed very successfully from its early beginnings in the 1940s, at which time it was mainly subject to research in the labs of a few physicists, to its present frequent use by a broad community. Widespread use of NMR started in the 1960s when instruments moved into the laboratories of chemists to support analytics of synthesized products. The progress of modern chemistry only became possible with the advent of powerful analytical instrumental methods, with NMR spectroscopy playing a very pivotal role amongst them. To understand the importance of NMR, we only need to look back on natural product synthesis prior to the advent of NMR, where all intermediates had to be compared to known compounds through chemical transformations. Today, NMR is not only used by chemists, but also by researchers working in material science, structural biologists, the pharmaceutical industry, in product quality control as well as in many more fields of application.

Considering the importance of NMR in many branches of chemistry basic NMR knowledge is traditionally taught in the chemistry curriculum, and this is often done in combination with other spectroscopic techniques such as IR, UV, or MS. The content of these courses primarily aims at providing the student with practical skills of how to elucidate the structure of small (usually organic) molecules from simple spectra, mostly 1D and simple 2D spectra. Accordingly, the necessary empirical knowledge for example typical chemical shifts for important compound classes are taught, whereas the physicochemical background on the nature of the chemical shifts is less frequently explained. A reader interested in these topics is faced with a plethora of very good NMR books. However, these books generally aim at a readership with more advanced knowledge in physical chemistry and quantum mechanics, and as a result the reader may have difficulty understanding the presented topics.

NMR has rapidly moved into adjacent branches of science and today it is not only chemists that come into contact with NMR. Modern molecular biology makes heavy use of NMR to understand the structure and dynamics of biological macromolecules such as proteins, nucleic acids, or oligosaccharides. Today, some of the top Bio-NMR groups are hosted in the biological sector. NMR is also being increasingly applied in pharmaceutical sciences, both in the academic as well as in the industrial environment. Physicists also use NMR, often solid-state techniques, to

probe for properties of materials; and last but not least NMR experiments are performed in industrial labs worldwide.

We have written this book as an introduction to NMR for scientists in the above-mentioned fields. A guiding principle of the book is to introduce a topic first in very simple terms, and then to reexamine the topic at more elevated levels of theory. Thereby we hope to provide the reader with a source of knowledge that bridges the gap to the more advanced NMR books. We feel that the taught content and level of theoretical detail should be sufficient for a chemistry student at all levels, including those undertaking a PhD thesis unless the thesis topic is directly related to NMR. Of course, the reader is strongly encouraged to consult more advanced NMR textbooks, since we cannot cover all theoretical details in this book.

Twenty years ago samples were usually handed over to an NMR department and the spectroscopist would have returned processed and often also interpreted spectra. Since that time the situation has changed significantly to one where all these steps are performed by the students themselves. At the University of Zurich students are taught how to record their own NMR spectra, and they have hands-on experience of the spectrometers from the second year of their studies onwards. The stability of modern NMR spectrometer equipment and software has enabled nonexpert users to use NMR and easily perform more advanced 2D or even 3D NMR experiments. We feel, however, that it is important that the technical aspects of NMR are properly understood. The first steps in setting up an experiment are usually locking, shimming, probehead tuning etc., and although these steps are now often done automatically by the spectrometer we feel that it is unsatisfactory if users do not properly understand the actual meaning of these steps. Also of tremendous importance is correct spectra processing, and again, this is currently mostly done by the students themselves.

The book begins with a short basic introduction to solution NMR for the novice and explains the meaning of chemical shift and scalar couplings whilst also demonstrating how a small organic compound is readily identified from simple 1D spectra. The basics of NMR are then covered in the next part of the book with the second chapter reexamining the basic topics in more detail while also describing practical aspects of sample preparation, referencing etc. The third chapter provides an in-depth account of proton NMR spectroscopy, containing much of the empirical knowledge required for proton spectra interpretation. Following on from this we provide a similar account for ^{13}C and other X nuclei.

The second part of the book then presents the theory of NMR at a more advanced level, from single spins to macroscopic magnetization. It also describes the origin of the chemical shift and scalar couplings, and introduces the product operator formalism which is currently the most common technique to describe NMR experiments. This part finishes with a brief introduction to the quantum-mechanical description of NMR, and whilst this may prove too advanced for the novice reader, we considered it important for those readers that would like to consult the primary literature on NMR. The chapter introduces the meaning of many technical terms used in the field and may help in bridging the gap to the more advanced NMR books. Should students feel that they can successfully read the classical NMR liter-

ature after having read our book then we would certainly be very happy. Particularly in this last chapter we have excluded a lot of material for which the interested reader is referred to the more advanced NMR books or the original literature.

The third part of the book is devoted to the technical aspects of NMR, providing an overview of the instrument, spectra processing methods, and going into detail on spectra acquisition. Important experiments are described as well as features of pulses, gradients etc. For readers looking for more detail on the NMR experiments we have also added a chapter on the architecture of pulse programs.

The fourth part is devoted to special topics in NMR. It introduces important topics such as relaxation, the nuclear Overhauser effect, exchange phenomena, two-dimensional NMR, solid-state NMR, and the detection of intermolecular interactions by NMR (often referred to as screening in industry).

A good understanding of basic theory and the available set of experiments is certainly required, however the prime goal of NMR is still to correctly elucidate the chemical structure of a compound and this requires solid knowledge of empirical rules and an overview of the available NMR methods and experiments. Often the set of experiments that are most helpful for a particular task depend on the class of compound, and will be different, for example, for a peptide compared to an alkaloid. In this regard we present in the fifth part of the book a few important classes of natural products (carbohydrates, steroids, peptides, and nucleic acids). Each chapter begins with a brief summary of important chemical and structural features of the molecules concerned, provides summaries of typical chemical shifts, and suggests suitable strategies to most efficiently assign compounds from that class. Finally, an interpretation of a representative example from the class in question is provided on the basis of 1D and 2D spectra. PDF files of all spectra for enlargement are available under www.chem.uzh.ch/static/nmrbook. We will also publish corrections under this link.

This book was written with the invaluable help of many friends, who provided advice on the content of chapters and helpful criticism on how the material is presented. Any remaining errors are entirely our fault. We are particularly thankful to Stefan Berger, Sebastian Benz, Marcel Blommers, Fred Damberger, Marc-Olivier Ebert, Matthias Ernst, Thomas Fox, Gerd Gemmecker, Roland Hany, Erhard Haupt, Jan Helbing, Bernhard Jaun, Henning Jacob Jessen, Silke Johannsen, Ishan Calis, Wiktor Kozminski, Andrea Mazzanti, Frank Löhr, Detlef Moskau, Kerstin Möhle, David Neuhaus, Bernhard Pfeiffer, Daniel Rentsch, Alfred Ross, Markus Vöhler, Reto Walser, and Gerhard Wider. Nadja Bross helped with the preparation of the figures, measuring spectra, and critical reading of the chapters. Finally, we would like to thank our families for their patience.

Zurich, August 2013

Simon Jurt and Oliver Zerbe

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