国外化学经典教材系列（影印版）

5

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Mass Spectrometry
(2nd Edition)

Jürgen H. Gross

原著第2版

科学出版社

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Foreword

Shortly after having graduated in 1966 and just employed as a research assistant in a protein chemistry laboratory, my very first contact with mass spectrometry happened when I stumbled on a paper by Michael Barber, the later discoverer of fast atom bombardment (FAB). Together with a French group he had determined the covalent structure of an almost 1.4 kDa complex peptidolipid called fortuitine by using mass spectrometry. Fascinated by this to me unknown technique, I felt that MS would be a future key analytical method in protein studies. At that time, the only ionization method available was electron ionization, which required a sample to be in the gaseous state in the ion source. Therefore most mass spectrometric analyses were dealing with small organic molecules – and peptides and proteins were not volatile. Fortuitine was a very fortuitous sample, because it was naturally derivatized with the consequence that it could be volatilized into the ion source. Nevertheless, I went into mass spectrometry. My first mass spectrometer was installed in our laboratory in 1968. Mass spectrometers at that time were complex fully manually operated instruments most of them magnetic/electrostatic sector instruments, and the operator needed to know the instrument well in order to avoid catastrophes by opening wrong valves at the wrong moment. Spectra were recorded on UV paper with a galvanometer recorder or on photographic plates and mass assignment was performed manually. During the 1970s a number of new ionization methods and mass analyzers became available. These included ionization by chemical ionization and by field ionization/desorption as well as mass analyses by quadrupoles and ion traps. Computers became available for data acquisition and mass assignment. Life became easier but the requirement for volatile samples was still there.

The 1980s revolutionized the possibilities for mass spectrometric analysis. In the early half of the decade introduction of FAB and commercialization of the 10 years earlier developed plasma desorption mass spectrometry allowed for analyses of nonvolatile samples such as peptides, proteins, and nucleic acids. The first commercial fully automated mass spectrometer, the BioIon plasma desorption mass spectrometer, became available and the time-of-flight analyzer, which had unlimited mass range, was revived. Late in the decade the two new and now dominating ionization methods electrospray ionization (ESI) and matrix-assisted laser desorption ionization (MALDI) were introduced. These two ionization methods opened a new era for mass spectrometry. Now all the large nonvolatile biological molecules could be analyzed. Till then GC-MS had been extensively used for analysis of complex mixtures in environmental and clinical sciences, but due to its nature it was limited to small volatile molecules. ESI made coupling of LC with MS possible allowing for entirely new applications of mass spectrometry. Proteomics now became a big move forward with mass spectrometry as the key analytical tool. Thousands of scientists took up mass spectrometric analysis and

the instrument manufacturers realized that a new market had emerged and that the new generation of users were different from the previous technically skilled specialists. The new generation of instruments therefore became computer controlled, equipped with safety features to avoid any erroneous operation and with fully computerized data acquisition. The requirement from the biological sciences for high speed, sensitivity, and mass accuracy resulted in dramatic improvements of the performance of the instruments. Hybrid instruments combining the well-known mass analyzers were constructed, the FT-ICR mass spectrometer, which till then had only been available in highly specialized mass spectrometry laboratories, moved into the biological laboratory. Lately, the orbitrap analyzer, also based on Fourier transformation, has become standard in advanced biological research laboratories. Biological mass spectrometry and especially analysis of proteins and proteomics now dominate mass spectrometry conferences and mass spectrometry has a strong position in biological conferences, where these subjects ten years earlier were only marginally present.

What are the consequences of this development? For me, having tried to get mass spectrometry into protein science for more than 40 years it is of course encouraging. Mass spectrometry is without any doubt now the most versatile analytical technique available. It is used in a wide variety of areas from inorganic, nuclear chemistry, and geochemistry over organic chemistry, environmental analyses, clinical chemistry, to molecular and cell biology. Online separation of complex mixtures is possible using either GC-MS or LC-MS. Almost all commercial instruments are highly automated. However, this development also rises serious concerns. Many of the new users consider the mass spectrometer as a black box where they put in the sample in one end and get a result from the computer in the other end. They do not or only marginally understand the principles in their instrument and rarely look at the raw data. They are satisfied with computer prints with lists of identified compounds. Sample preparation often follows standard protocols and the understanding of the need for optimized sample preparation for each analytical task is often ignored. As a result, a considerable amount of the data obtained are questionable either due to poor sample preparation, poor instrument performance, or suboptimal use of the instruments. It is my wish that the new generation of mass spectrometry users will spend time to understand their instruments and the requirements for optimal preparation of the samples and it is my hope that this book will be read by many of them so that they can use their techniques to the best of the equipment's potential.

Odense, 2010

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Preface to the Second Edition

To all readers of the first edition of *Mass Spectrometry – A Textbook* I would like to express my deepest gratitude. Without their interest in wanting to learn more about mass spectrometry by use of this book, all the efforts in writing it would have been a mere waste of time, and moreover, without their demand for updates, there would be no next edition. I would also like to thank the instructors all over the world who adopted and recommended this book for their own mass spectrometry courses.

Preparing the second edition of *Mass Spectrometry – A Textbook* was not an easy task. The years have witnessed a flood of innovations and detailed knowledge of interrelationships that were previously hardly understood. The time between the editions may have appeared a bit long for many eager scholars. But the author has used the time effectively to improve and update the entire contents, hopefully to the benefit of all who have been patiently bearing with me in anticipation.

So, what's new? The book now comprises fifteen instead of twelve chapters, each of them headed by essential "Learning Objectives". Chapter 9 inserts methods of ion activation such as CID, ECD, ETD, and IRMPD closely related to the instrumental approaches to tandem mass spectrometry. A second additional chapter deals with sampling and ion generation from surfaces under ambient conditions as afforded by DART and DESI, to name the most relevant methods. Finally, a new chapter on inorganic mass spectrometry has been added, for one, to include element speciation that bridges the gap between biomedical and trace elemental analysis and, also, to open a perspective extending beyond the key topics of this book. The chapter on instrumentation has been significantly expanded to cover orbitrap, linear ion traps, TOF/TOF, FT-ICR, and the ever-changing hybrid instruments including IMS-MS systems. More detailed attention is drawn to applications regarding biopolymers, especially in those chapters dealing with MALDI and ESI.

Overall, the book has been expanded by more than 200 pages. No chapter has remained untouched. Numerous passages have been rewritten to improve the clarity of explanations while keeping them short and concise. Care has been taken not only to explain how, but also to why things are done a certain way. Several schemes have been added to clarify interrelationships between different techniques. Tables compiling data for general reference where transferred to the expanded appendix. The book's website has been updated providing new exercises and supplementary material (http://www.ms-textbook.com).

Many kind people have supported me in the process of compiling this second edition. I appreciate the detailed knowledge and great thoroughness of Kenzo Hiraoka, Yasuhide Naito, Takemichi Nakamura, and Hiroaki Sato allocated to the translation of the first edition into Japanese. The valuable and welcome comments from readers from all over the world, and in particular, from book reviewers and colleagues have revealed some shortcomings in the first edition, which now have been eliminated to the improvement of the resulting new edition.

As in the first edition, several well-respected colleagues have contributed to this book by carefully checking contents in their fields of expertise. For the second edition, I want to express special thanks to Jürgen Grotemeyer, Universität Kiel, for checking Chap. 2 (*Principles of Ionization and Ion Dissociation*), Alexander Makarov, Thermo Fisher Scientific, Bremen (Chap. 4, *Instrumentation*), Christoph A. Schalley, Freie Universität Berlin (Chap. 9, *Tandem Mass Spectrometry*), Belá Paizs, German Cancer Research Center, Heidelberg (Chap. 11, *Matrix-Assisted Laser Desorption/Ionization*), Zoltán Takáts, Universität Gießen (Chap. 13, *Ambient Mass Spectrometry*), and Detlef Günther, ETH Zürich (Chap. 15, *Inorganic Mass Spectrometry*). Without their care and help the many new parts would not have reached the present level of accuracy. Despite intense reviewing and proofreading some errors inevitably may have remained. I apologize for these in advance and would highly appreciate any feedback from the readership in trying to identify and correcting them.

I am indebted to Peter Roepstorff, Odense University, for writing the Foreword with such a personal connotation. Permission to prepare this 2nd edition, alongside my official professional duties, by A. Stephen K. Hashmi, Director of OCI, and Heinfried Schöler, Dean of the Faculty of Chemistry and Earth Sciences is sincerely acknowledged. Many thanks to Doris Lang, Iris Mitsch, and Norbert Nieth, for smoothly running the routine analyses in our MS facility. And again, several mass spectrometry companies are acknowledged for supplying new instrument schemes and other figures for inclusion in the 2nd edition. Theodor C. H. Cole accomplished a great job in polishing up my English. Finally, I am immeasurably grateful to my family for their patience and solidarity in times when I had to come home late or needed to vanish on Saturdays during the writing of this book.

Have a good time studying, learning, and enjoying the world of mass spectrometry!

Heidelberg, 2010

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Preface

When non-mass spectrometrists are talking about mass spectrometry it rather often sounds as if they were telling a story out of Poe's *Tales of Mystery and Imagination.* Indeed, mass spectrometry appears to be regarded as a mysterious method, just good enough to supply some molecular weight information. Unfortunately, this rumor about the dark side of analytical methods reaches students much earlier than their first contact with mass spectrometry. Possibly, some of this may have been bred by mass spectrometrists themselves who tended to celebrate each mass spectrum they obtained from the gigantic machines of the early days. Of course, there were also those who enthusiastically started in the 1950s to develop mass spectrometry out of the domain of physics to become a new analytical tool for chemistry.

Nonetheless, some oddities remain and the method which is to be introduced herein is not always straightforward and easy. If you had asked me, the author, just after having finished my introductory course whether mass spectrometry would become my preferred area of work, I surely would have strongly denied. On the other hand, J. J. Veith's mass spectrometry laboratory at Darmstadt University was bright and clean, had no noxious odors, and thus presented a nice contrast to a preparative organic chemistry laboratory. Numerous stainless steel flanges and electronics cabinets were tempting to be explored and – whoops – infected me with CMSD (chronic mass spectrometry disease). Staying with Veith's group slowly transformed me into a mass spectrometrist. Inspiring books such as *Fundamental Aspects of Organic Mass Spectrometry* or *Metastable Ions*, out of stock even in those days, did help me very much during my metamorphosis. Having completed my doctoral thesis on fragmentation pathways of isolated immonium ions in the gas phase, I assumed my current position. Since 1994, I have been head of the mass spectrometry laboratory at the Chemistry Department of Heidelberg University where I teach introductory courses and seminars on mass spectrometry.

When students ask what books to read on mass spectrometry, there are various excellent monographs, but the ideal textbook still seemed to be missing – at least in my opinion. Finally, encouraged by many people including P. Enders, Springer-Verlag Heidelberg, two years of writing began.

The present volume would not have its actual status without the critical reviews of the chapters by leading experts in the field. Their thorough corrections, remarks, and comments were essential. Therefore, P. Enders, Springer-Verlag Heidelberg (*Introduction*), J. Grotemeyer, University of Kiel (*Gas Phase Ion Chemistry*), S. Giesa, Bayer Industry Services, Leverkusen (*Isotopes*), J. Franzen, Bruker

Daltonik, Bremen (*Instrumentation*), J. O. Metzger, University of Oldenburg (*Electron Ionization* and *Fragmentation of Organic Ions and Interpretation of EI Mass Spectra*), J. R. Wesener, Bayer Industry Services, Leverkusen (*Chemical Ionization*), J. J. Veith, Technical University of Darmstadt (*Field Desorption*), R. M. Caprioli, Vanderbilt University, Nashville (*Fast Atom Bombardment*), M. Karas, University of Frankfurt (*Matrix-Assisted Laser Desorption/Ionization*), M. Wilm, European Molecular Biology Laboratory, Heidelberg (*Electrospray Ionization*) and M. W. Linscheid, Humboldt University, Berlin (*Hyphenated Methods*) deserve my deep gratitude.

Many manufacturers of mass spectrometers and mass spectrometry supply are gratefully acknowledged for sending large collections of schemes and photographs for use in this book. The author wishes to express his thanks to those scientists, many of them from the University of Heidelberg, who generously allowed to use material from their actual research as examples and to those publishers, who granted the numerous copyrights for use of figures from their publications. The generous permission of the National Institute of Standards and Technology (G. Mallard, J. Sauerwein) to use a large set of electron ionization mass spectra from the NIST/EPA/NIH Mass Spectral Library is also gratefully acknowledged. My thanks are extended to the staff of my facility (N. Nieth, A. Seith, B. Flock) for their efforts and to the staff of the local libraries for their friendly support. I am indebted to the former director of our institute (R. Gleiter) and to the former dean of our faculty (R. N. Lichtenthaler) for permission to write a book besides my official duties.

Despite all efforts, some errors or misleading passages will still have remained. Mistakes are an attribute that make us human, but unfortunately, they do not contribute to the scientific or educational value of a textbook. Therefore, please do not hesitate to report errors to me or to drop a line of comment in order to allow for corrections in a future edition.

Hopefully, *Mass Spectrometry – A Textbook* will introduce you to the many facets of mass spectrometry and will satisfy your expectations.

Heidelberg, 2003

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