



### Reactive Intermediates

This book highlights one of the increasingly diverse fields of application of “modern” mass spectrometry, namely the identification and characterization of reactive intermediates involved in chemical reactions in solution.

The research described in the book is based on the electrospray ionization (ESI) technique, which—eight years after its inventor Professor John Fenn was awarded the Nobel Prize in Chemistry—is now one of the most important and firmly established ionization methods of applied mass spectrometry. It is well known that ESI-MS allows us to identify salts and polar (and often high-mass) compounds by direct transfer of their ions from solution into the gas phase. It has been shown that, because of the high specificity and low detection limits of mass spectrometry, ESI-MS makes it possible to detect and characterize short-lived reactive intermediates, even at concentrations several orders of magnitude lower than those of the stable reactants and products. This book collects—for the first time as far as I know—many results from this novel, exciting, and inspiring application of mass spectrometry, which aims at a better understanding of (mostly organic) chemical reactions in solution. It provides a good overview of the development of the field during the past 10–15 years.

One of the virtues of this book is that it includes wide-ranging discussions of the basic principles of ESI mass spectrometry. These are presented in three of the eight chapters. Thus, in Chapter 1, P. Kebarle and U. H. Verkerk provide a good overview of the ESI method and the mechanistic models of the ESI process. In Chapter 2, H. Chen gives a brief but informative outline of the historical development of mass spectrometric methods: “from the gas phase [back] to solution”. In Chapter 8, K. A. Schug contributes a somewhat more specialized article on the application of ESI-MS to the investigation of noncovalent (bio)-molecular recognition processes in solution. Also, in Chapter 5, as part of his own contribution, the editor describes several ESI-MS methods developed for the on-line monitoring of species present in reacting systems (including reactive intermediates).

However, the main emphasis of the book is on the comparison of results obtained by ESI-MS investigations of reacting solutions with knowledge and theories about the mechanisms underlying the widely different chemical reactions. In Chapter 3, F. M. Nachtigall and M. N. Eberlin report on various such topics, including the Morita–Baylis–Hillman reaction, the  $\alpha$ -methenylation of ketoest-

ers, the Heck, Suzuki, and Stille cross-coupling reactions,  $S_NAr$  and other substitution reactions, Fenton reactions, the Biginelli dihydropyrimidine synthesis, and other ring-closure processes. In Chapter 4, Y. Guo and co-authors describe intermediates that have been detected by ESI-MS in various palladium-catalyzed cross-coupling reactions, radical-cation-induced cycloaddition reactions, and transition-metal-catalyzed polymerization reactions. In Chapter 5, L. S. Santos contributes the by far most comprehensive (and, in comparison, more critical) discussion in this collection of articles. Besides the many reactions already mentioned above, he comments on various photo-initiated processes, on epoxidation reactions and other oxidative conversions (of coffee and isoprene, for example), and on Ziegler–Natta-type polymerizations carried out in different reaction systems. In Chapter 7, A. Roglans and A. Plaquintana focus their contribution on the numerous palladium-containing intermediates in Suzuki–Miyaura, Mizoroki–Heck, and Stille reactions, as well as in related cross-coupling and palladium-catalyzed polymerization reactions, which were observed by means of ESI mass spectrometry.

From an organic-chemical point of view, all these chapters present a multifaceted field of research. Through the mechanistic reaction schemes, mass spectra, and tabulated data, the reader is provided with concrete information about the detection of numerous intermediates in solution, corroborating or even confirming reaction mechanisms that, admittedly, had been suggested previously. Therefore, large parts of this book describe a collection of ionic species that have been observed by mass spectrometry in the gas phase, and to which a definite role in the course of chemical reactions can be attributed.

Investigations that go beyond the mere detection of ions—such as the structural characterization of the gaseous ions (e.g., by collision experiments, MS<sup>n</sup>) on the basis of comparison with “authentic” ions, and experiments to determine their reactivity with neutral reaction partners in vacuo (by ion/molecule reactions, IMR)—are not covered in depth in the book. At least, however, studies of this kind carried out on radical chain reactions and on Ziegler–Natta polymerization by J. O. Metzger and co-authors, and on ruthenium-catalyzed metathesis reactions by P. Chen and co-authors, are mentioned.

In this context, R. A. J. O’Hair presents a well-directed and highly informative contribution on gas-phase ion chemistry, discussing the generation and isolation of selected metal-containing ions by ESI mass spectrometry and their subsequent “demasking” by gas-phase collision experiments (Chapter 9). This chapter demonstrates, in a very systematic and exemplary manner, how reactive



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metal-containing intermediates can be generated from gaseous precursor ions by MS/MS or MS<sup>3</sup> experiments. Thus, in contrast to the previous chapters, pure gas-phase ion chemistry is highlighted here, albeit without concrete reference to any of the condensed-phase reactive intermediates discussed in the other chapters.

A number of important points of criticism should not be ignored. The book contains an unacceptably large number of chemical errors and other mistakes, not only in the text but, irritatingly, mainly in the schemes. In more than one case, the symbol “Pd” appears instead of “Ph” in a [(2-phenylallyl)palladium]<sup>+</sup> complex. In some of the chapters that report on the “fishing” of reactive intermediates from solution by ESI-MS, “swarms” of errors occur, and even carefully written chapters contain some mistakes. Moreover, the fact that the editor, in his preface, names one of the peers of mass spectrometry, Professor R. G. Cooks, as a contributing author, whereas he does not appear as such throughout the book, is more than astonishing.

Parts of this book are written in a rather wordy style, others in a somewhat diffuse manner.

Although the enthusiasm of the authors for their subjects is clear, considerable shortening would have improved the contributions. In my view, it is particularly questionable to discuss the same chemical reactions repeatedly in several chapters, without achieving any deeper insight! This weak point, and the numerous mistakes, should be corrected in a revised edition.

Notwithstanding these drawbacks, the book offers valuable information on the analysis of the mechanisms and reactive intermediates involved in organic reactions by means of ESI mass spectrometry. It will certainly provide a useful guideline for future research into this new field of mass spectrometry applied to the fundamentals of organic chemistry.

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