

Preface

Ion/molecule reaction mass spectrometry has proved to be one of the most powerful, sensitive, and versatile research techniques and has been applied to analysis in a great variety of qualitative and quantitative studies. As a consequence, mass spectrometers have undergone endless cycles of development of ionization methods for a wide variety of applications. Under these circumstances, the novel ionization method appears that must make difference in science, especially in the field of chemical and environmental analysis, plasma diagnostics, process monitoring, biological, and clinical analysis.

The study of ion–molecule reactions started in the early 1950s with active researches in conventional mass spectrometers with modified ion sources operated at high pressure. Its unique feature is that the initial reaction step is driven by ion–permanent dipole or ion-induced dipole attraction between the reactants and it often occurs without any activation energy. The field has grown rapidly since that time. Pioneering works go back to experiments of Talrose and Melton and the technique was developed to be analytically useful by Munson and Field in the mid-1960s. Kinetic and thermodynamic studies have also grown rapidly during that time, with the development of mass spectrometry (MS) itself. Indeed, the majority of the thermochemical parameters in the gas phase for chemical compounds were determined using various MS techniques.

The ion–molecule association reaction is one of the various reaction types observed in ion–molecule reactions. It is a unique process similar to the combination of two atoms or two free radicals. The energy accumulated in the reaction complex often must be liberated by collision with a third body for the complex to survive. Studies of complex ions are relevant to phenomena such as solvation, clustering, plasma chemistry, radiation chemistry, flame and combustion, and even atmospheric and interstellar processes. The research area has been extended to the subject of a clustered ion formation in bridging the gap between the gas and condensed phase.

The characterization of reactive intermediate, free radical has been one of the most important challenges for the scientist in the history of chemistry. In early times, MS has appeared as a direct method to study radical intermediates due to its immediate response in the analysis. Among the various original methods developed in the purpose of detecting and characterizing free radicals in dynamic chemical systems such as plasmas and combustion, the ion attachment mass spectrometry

(IAMS) method to exploit alkali ion/molecule association reaction (cationization) appears to be an alternative to low-energy electron impact ionization methods. A real challenge for IAMS is to extend its capability to detect intermediary free radical species in various dynamic chemical systems. Recently this type of mass spectrometer is available commercially in a complete form.

Transition to the Gaseous to the Condensed Phase A variety of ionization techniques in the condensed phase are now available which enable MS to be used for the direct analysis of nonvolatile or/and thermally labile compounds. These include field desorption (FD), fast atom bombardment (FAB), plasma desorption (PD), secondary ion mass spectrometry (SIMS), electrospray ionization (ESI), and laser desorption (MALDI). Most methods can be classified into desorption ionization (DI). Cationization reactions are ubiquitous in DI MS, where traces of alkali salts are often sufficient to produce intense cationized species. Cationization appears to hold great promise for the analysis of nonvolatile and thermally labile compounds. Studies have been extensively done to understand the mechanism of this form of ionization in order to make a wider application of the technique. Cationization MS has already been regarded as the method of choice for the analysis of nonvolatile and thermally labile substances. Thus, the questions arise: (1) what are the distinct features of cationization MS, (2) what are problems of the technique and (3) what is its advantage for the analysis of biological substances, drugs and drug metabolites, medicinal and environmental chemicals. Gas-phase ion/molecule reaction chemistry can potentially lead to the understanding of the ion complexation (cationization) mechanism in the condensed phase. To our best knowledge, so far, no comprehensive monograph has been published for the basic fundamentals of ion/molecule association reaction and its mass spectrometric applications (conditions) for a wide diversity of analytical study.

Characteristics of This Book This monograph will cover primarily thermal alkali-metal ion association reactions of the general type: $A^+ + M + N \rightleftharpoons (A+M)^+ + N$, where A denotes a positively charged alkali metal ion, M is a neutral species and N works as a third body. In this volume, nine chapters are presented. They include tutorials on important principles as well as reviews on special topics, covering fundamental operating principles, instrumentation, and representative applications for all areas of chemical dynamics, environmental chemistry, molecular medicine, and biological science. Cationization is defined (used) in this book as metal ion association, both in the gas-phase and in the condensed-phase. Attachment and association are used interchangeable. Other synonyms are listed elsewhere. Authors try to prepare the manuscript for reader to find a guide for tomorrow by taking lessons from the past. In other words, this book includes rather old but excellent studies, which seems to be obsolete. Individual chapters will be available for purchase from the publisher's website. In order for these chapters to be self-completed, it is inevitable to have few replications. Consequently, each chapter contains references to research articles and reviews.

This book is divided into nine parts:

1. Introduction
2. Ion chemistry (principle)
3. A theoretical approach to ion-molecule complexation
4. Experimental methods and instrumentation
5. Applications of association reactions in the gas-phase
6. Hybrid system with ion attachment techniques
7. Cationization MS for the condensed-phase samples
8. Direct analysis mass spectrometry
9. Future prospects

Chapter 1 provides a historical viewpoint (perspective) on the study of ion/molecule association (cationization) MS as well as explanation on the evolution of developments of the instrumental methods. In addition to serving as an introduction for the subject of cationization MS as it pertains to ion chemistry, this chapter briefs thermochemistry and chemical dynamics (and analytical application) of metal ion association reaction. The fundamentals for ion/molecule association reaction are described in *Chapter 2*, providing a basic introduction to the mechanism and dynamics of termolecular association reaction, dissociation and fragmentation reaction of associated ion and ion/molecule association mechanism in the condensed-phase.

Chapter 3 briefly describes the basic concepts behind ion-molecule interactions, such as ion-dipole, ion-induced dipole, and ion- π interactions. Fundamental theories explaining ion-molecule association/dissociation reaction dynamics are also outlined in this chapter. Computational methodologies to study the ion-molecule interactions are discussed. Finally, theoretical studies (using both *ab initio* and density functional theories) on ion interactions with organic molecules, biomolecules, and materials are given in detail with a lot of important and fundamental examples.

Chapter 4 discusses a variety of experimental methods and introduces instrumentation for the study of gas-phase ions and ion-molecule chemistry in general and of ion attachment processes in particular, with an emphasis on mass spectrometry (MS) methods. The section starts with a discussion on common methods to generate gas-phase alkali metal ions, to be applied in various ion-attachment experiments. Subsequently, (tandem) MS methods are discussed that enable the investigation of the structure of ions and the results of ion-molecule reactions. Separate sections are presented for beam instruments and ion-trapping instruments. In some cases, these instruments can be used to perform ion-molecule reactions as part of the measurement protocol. Emphasis is put on commercial available MS and MS-MS instruments. In subsequent sections, various other tools are discussed, that may be combined with MS and allow the study of gas-phase reactions of ions. These tools comprise (a) flowing-afterglow methods (FA-MS), including derived methods like selected-ion flow tubes (SIFT-MS) and proton-transfer reaction devices (PTR-MS), (b) drift tubes, ion-mobility spectrometry (IMS) and IMS-MS, and (c) high-pressure MS instruments. The text provides ample references for further reading.

Chapter 5 explores the application of alkali-metal ion/molecule association in the gas-phase to MS. This chapter: (1) surveys the fundamental basis to build the

instrument, (2) describes the instrumentation to the measurement of mass spectrum, and (3) summarizes mass spectrometric applications to measurements on chemical compounds, which include intermediary free radical, interstellar, environmentally important, and unfamiliar or unstable species. The subject of application of the restriction of hazardous substances (RoHS) directive is also covered.

Chapter 6 describes the concept of hybrid mass spectrometric system with ion attachment technique as ionization method. A combined (hyphenated) MS represents time-of-flight (TOF), ion trap quadrupole, ion mobility spectroscopy, ion cyclotron resonance (ICR) or aerosol MS, while descriptions of specially designed inlet system include chromatographic introduction (inlets), and various pyrolysis probes for evolved gas analysis. Some applications of each technology are presented, together with representative and/or illustrative examples. In addition, development of portable IAMS is provided along with explanations and spectral applications.

Chapter 7 highlights analytical mass spectrometry with use of Alkali metal ion reaction (association) in the condensed-phase. Methodology for cationization MS is emphasized in this chapter, which also describes role of M^+ adduct of biologically important nucleosides, peptide or protein, sugars, as well as synthetic polymers. The approach and procedure for the structural characterization of biologically important substances from CID, BIRD, ECD, ISD and PSD MS/MS data, are described in detail, being reviewed by hundreds of current topics.

Chapter 8: Recently, we have seen a rapid development in direct introduction mass spectrometry (DIMS). Among the DIMS instruments mentioned are: atmospheric-pressure chemical ionization (APCI), proton-transfer-reaction mass spectrometry (PTR-MS), selected ion-flow-tube mass spectrometry (SIFT-MS), ion-molecule reaction mass spectrometry (IMR-MS), direct analysis in real time (DART) and desorption electrospray ionization (DESI). These technologies are also compared for applications to ambient mass spectrometry. Finally, selected examples of applications for the technologies are given, including research monitoring of volatile organic compounds (VOCs) in the applications to food-quality control, flavor release, process monitoring, environmental and medical sciences.

Chapter 9 discusses IAMS from the application point of view, highlighting important contributions IAMS can make in the study of dynamic systems like flames, discharges and plasmas, in pharmaceutical, biochemical and biotechnological, environmental, food safety, and polymer application areas.

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