Contents

Foreword XIII Preface XXI List of Contributors XXIII

| 1 | A Brief Overview of the Mechanisms Involved in Electrospray |
|--------|--|
| | Mass Spectrometry 1 |
| | Paul Kebarle and Udo H. Verkerk |
| 1.1 | Introduction 1 |
| 1.1.1 | Origins of Electrospray Mass Spectrometry 1 |
| 1.1.2 | Aims of this Chapter 2 |
| 1.2 | Production of Gas-Phase Ions by Electrospray and Electrospray |
| | Ionization Mass Spectrometry 3 |
| 1.2.1 | Overview 3 |
| 1.2.2 | Production of Charged Droplets at the Capillary Tip 5 |
| 1.2.3 | Electrospray as an Electrolytic Cell 7 |
| 1.2.4 | Required Electrical Potentials for ES. Electrical Gas Discharges 8 |
| 1.2.5 | Current, Charge and Radius of Droplets Produced at the |
| | Capillary Tip 10 |
| 1.2.6 | Solvent Evaporation from Charged Droplets Causes Coulomb |
| | Fissions of Droplets 10 |
| 1.2.7 | Evaporation of Droplets Leading to Coulomb Fissions Producing |
| | Progeny Droplets that Ultimately Lead to Ions in the Gas-Phase; |
| | Effects of the Concurrent Large Concentration Increase 11 |
| 1.2.8 | Mechanism for the Formation of Gas-Phase Ions from Very Small |
| | and Highly Charged Droplets. The Ion Evaporation Model (IEM) |
| 1.2.9 | Observed Relative Ion Intensity of Small Analytes. Dependence |
| | on the Nature of the Analyte, its Concentration and Presence of |
| | Other Electrolytes in the Solution. High Sensitivities of |
| | Surface-Active Analytes 17 |
| 1.2.10 | Large Analyte Ions such as Dendrimers and Proteins are Most |

Probably Produced by the Charged Residue Model (CRM) 22

15

VIII Contents

| 1.2.11 | Nanospray and Insights into Fundamentals of Electro and |
|-------------|---|
| 1 2 1 2 | Nanospray 26 Consequences of the Increase in Concentration Caused by |
| 1.2.12 | Extensive Evaporation of Solvent in ESI Process. Promotion of |
| | - |
| 1 1 1 1 1 | 8 , |
| 1.2.12.1 | Positive-Negative Ion-Pairing Reactions Involving Impurities such as Na ⁺ 28 |
| 1 1 1 1 1 1 | |
| 1.2.12.2 | Determination of Equilibrium Constants in Solution via ESI-MS 29 References 31 |
| | |
| 2 | Historical Perspectives in the Study of Ion Chemistry by Mass |
| | Spectrometry: From the Gas Phase to Solution 37 |
| | Hao Chen |
| 2.1 | A Brief History and Recent Advances in Mass Spectrometry 38 |
| 2.1.1 | Early Developments 38 |
| 2.1.2 | Recent Advances 40 |
| 2.2 | Overview of the Study of Ion/Molecule Reactions in the Gas |
| | Phase by Mass Spectrometry 41 |
| 2.2.1 | Brief History 41 |
| 2.2.2 | Basic Types of Ion/Molecule Reactions 42 |
| 2.2.3 | Relationship to Reaction Analogies in Solution 43 |
| 2.2.3.1 | Mechanism Elucidation of Classical Organic Reactions 43 |
| 2.2.3.2 | Mechanism Elucidation of Organometallic Reactions 44 |
| 2.2.3.3 | Catalyst Screening 49 |
| 2.2.3.4 | Synthesis of Elusive Ionic Species 49 |
| 2.2.3.5 | Probing Reactivity of Microsolvated Cluster Ions 50 |
| 2.2.4 | Experimental Methods for the Study of Ion/Molecule Reactions 50 |
| 2.2.4.1 | Low-Pressure Ion/Molecule Reactions 50 |
| 2.2.4.2 | High-Pressure Ion/Molecule Reactions 51 |
| 2.3 | Future Perspectives 52 |
| | References 53 |
| 3 | Organic Reaction Studies by ESI-MS 63 |
| | Fabiane M. Nachtigall and Marcos N. Eberlin |
| 3.1 | Introduction 63 |
| 3.2 | Reaction Mechanisms 65 |
| 3.2.1 | Morita-Baylis-Hillman Reaction 65 |
| 3.2.2 | Morita-Baylis-Hillman Reaction Co-catalyzed by Ionic Liquids 67 |
| 3.2.3 | α-Methylenation of Ketoesters 71 |
| 3.2.4 | Unexpected Synthesis of Conformationally Restricted Analogs |
| | of γ -Amino Butyric Acid (GABA) via a Ring Contraction Reaction 73 |
| 3.2.5 | The Heck Reaction 75 |
| 3.2.6 | Suzuki Reaction 81 |
| 3.2.7 | Stille Reaction 81 |
| 3.2.8 | Three-Component Pd(0)-Catalyzed Tandem Double |
| | Addition-Cyclization Reaction 83 |

- 3.2.9 Alkynilation of Tellurides Mediated by Pd(II) 84
- 3.2.10 TeCl₄ Addition to Propargyl Alcohols 88
- 3.2.11 S_N2 Reactions 89
- 3.2.12 Allylic Substitution Reaction 91
- 3.2.13 Heterogeneous Fenton Reaction 93
- 3.2.14 Mimicking the Atmospheric Oxidation of Isoprene 93
- 3.2.15 Advanced Oxidation Processes of Environmental Importance 95
- 3.2.16 Tröger's Bases 96
- 3.2.17 The Three-Component Biginelli Reaction 98
- 3.2.18 Modeling the Ribonuclease Mechanism 103
- 3.2.19 Oxidative Cleavage of Terminal C=C bonds 105
- 3.3 General Remarks 108 References 108
- 4 Studies of Reaction Mechanism Intermediates by ESI-MS 113
 - Rong Qian, Jing Zhou, Shengjun Yao, Haoyang Wang, and Yinlong Guo
- 4.1 Introduction 113
- 4.2 Studies on the Intermediates and Mechanisms of Pd-Catalyzed Reactions *113*
- 4.3 Studies on Some Reactive Intermediates and Mechanisms of Radical Reactions *115*
- 4.4 Studies on the Intermediates and Mechanism of Organocatalysis Reactions 121
- 4.5 Studies on the Intermediates and Mechanism of Transition Metal-Catalyzed Polymerization Reactions 123 References 129
- 5 On-line Monitoring Reactions by Electrospray Ionization Mass Spectrometry 133

Leonardo S. Santos

- 5.1 Introduction 133
- 5.2 Preservation of the Charge in the Transit of Ions from Solution to the Gas Phase Using the ESI Technique 134
- 5.3 Developing Methods to Study Reaction Mechanisms 135
- 5.3.1 Monitoring Methods 135
- 5.3.1.1 Off-Line Monitoring 135
- 5.3.1.2 On-Line Monitoring 136
- 5.3.2 Microreactors 136
- 5.3.2.1 PEEK Mixing Tee as Microreactor 136
- 5.3.2.2 Capillary Mixer Adjustable Reaction Chamber 137
- 5.3.2.3 Photolysis Cell 138
- 5.3.2.4 Photochemical Reactor 139
- 5.3.2.5 Nanospray Photochemical Apparatus 140
- 5.3.2.6 Electrochemical Cell 141
- 5.4 Probing Reactivity of Intermediates 142
- 5.4.1 Reaction Mechanism Studies 143

X Contents

| 5.4.1.1 | Radical Fenton Reaction 143 |
|---------|---|
| 5.4.1.2 | Heterogeneous Fenton System 144 |
| 5.4.1.3 | Radical Cation Chain Reactions 145 |
| 5.4.1.4 | [2 + 2]-Cycloaddition of Trans-Anethole 145 |
| 5.4.1.5 | Electron Transfer Initiated Diels–Alder Reactions 148 |
| 5.4.1.6 | Radical Chain Reactions 149 |
| 5.4.1.7 | Photochemical Reactions 151 |
| 5.4.1.8 | Photochemical Switching Reaction 151 |
| 5.4.1.9 | Photoinitiated Polymerization Reaction 153 |
| 5.4.2 | Electrochemical Reactions 154 |
| 5.4.3 | Heck Reaction 154 |
| 5.4.4 | Suzuki Reaction 156 |
| 5.4.5 | Pd-Catalyzed Enantioselective Allylation Reaction 156 |
| 5.4.6 | Stille Reaction 157 |
| 5.4.7 | Alkynilation of Tellurides Mediated by Pd(II) 158 |
| 5.4.8 | Lewis Acid-Catalyzed Additions 162 |
| 5.4.9 | C–H Activation and Hydrogenations 162 |
| 5.4.10 | Oxidation Reactions 163 |
| 5.4.11 | Epoxidation 164 |
| 5.4.12 | The Baylis-Hillman Reaction 166 |
| 5.4.13 | The Baylis-Hillman Reaction Co-Catalyzed by Ionic Liquids 167 |
| 5.4.14 | Ring Contraction Reaction 169 |
| 5.4.15 | Nucleophilic Substitution Reactions – The Meisenheimer |
| | Complex 169 |
| 5.4.16 | Oxidative Degradation of Caffeine 171 |
| 5.4.17 | Mimicking Atmospheric Oxidation of Isoprene 173 |
| 5.4.18 | α-Methylenation of Ketoesters 175 |
| 5.4.19 | Transient Intermediates of Petasis and Tebbe Reagent 176 |
| 5.4.20 | On-Line Screening of the Ziegler-Natta Polymerization |
| | Reaction 178 |
| 5.4.21 | On-Line Screening of the Brookhart Polymerization Reaction 181 |
| 5.4.22 | TeCl ₄ Addition to Propargyl Alcohols 181 |
| 5.4.23 | Mechanism of Tröger's Base Formation 186 |
| 5.5 | Conclusion 187 |
| | References 188 |
| | |
| 6 | Gas Phase Ligand Fragmentation to Unmask Reactive |
| | Metallic Species 199 |
| | Richard A. J. O'Hair |
| 6.1 | Introduction and Scope of the Review 199 |
| 6.2 | Unmasking Reactive Metallic Intermediates via Collision-Induced |
| | Dissociation 201 |
| 6.2.1 | Formation and Reactivity of Organometallics 201 |
| 6.2.1.1 | Formation and Reactions of Organolithium Ions 202 |
| 6.2.1.2 | Formation and Reactions of Alkaline Earth Organometalates 203 |
| | |

| 6.2.1.3 | Formation and Reactions of Organocuprates and Organoargentates 205 |
|-------------|--|
| 6.2.1.4 | Formation of Metal Carbenes 208 |
| 6.2.2 | Formation and Reactivity of Metal Hydrides 210 |
| 6.2.2.1 | Mononuclear Metal Hydrides 210 |
| 6.2.2.2 | Multinuclear Metal Hydrides 212 |
| 6.2.3 | Formation and Reactivity of Metal Oxides 215 |
| 6.2.3.1 | Bond Heterolysis 215 |
| 6.2.3.2 | Bond Homolysis of Metal Nitrites and Nitrates 216 |
| 6.2.4 | Formation and Reactivity of Metal Nitrides and Related Species 220 |
| 6.3 | Conclusions 224 |
| | References 224 |
| 7 | Palladium Intermediates in Solution 229 |
| | Anna Roglans and Anna Pla-Quintana |
| 7.1 | Introduction 229 |
| 7.2 | ESI-MS Studies in Suzuki-Miyaura Cross-Coupling and |
| | Related Reactions 231 |
| 7.3 | ESI-MS Studies in the Identification of Oxidative Addition |
| | Intermediates 237 |
| 7.4 | ESI-MS Studies in Mizoroki-Heck and Related Reactions 240 |
| 7.5 | ESI-MS Studies in Stille Cross-Coupling Reactions 251 |
| 7.6 | ESI-MS Studies in Palladium-Catalyzed Reactions |
| | Involving Allenes 254 |
| 7.7 | ESI-MS Studies in Palladium-Catalyzed Alkynylation Reactions 258 |
| 7.8 | ESI-MS Studies in Palladium-Catalyzed Allylic Substitution |
| P 0 | Reactions 260 |
| 7.9 | ESI-MS Studies in Palladium-Catalyzed Oxidation |
| H 10 | of 2-Allylphenols 268 |
| 7.10 | ESI-MS Studies in Palladium-Catalyzed Polymerization Reactions 269 |
| 7.11 | Conclusions 272 |
| | References 273 |
| 8 | Practical Investigation of Molecular and Biomolecular Noncovalent |
| | Recognition Processes in Solution by ESI-MS 277 |
| 0.1 | Kevin A. Schug |
| 8.1 | Introduction 277 |
| 8.2 | Methods and Applications 280 |
| 8.3 | Practical Aspects of Titration Analysis 290 |
| 8.4 | Summary and Outlook 298 |
| | References 298 |

Index 307