Preface

For a long time, mass spectrometry in organic chemistry was just used for the "fingerprint" identification of different compounds. Initiated by F.W. McLafferty and K. Biemann, and largely extended by C. Djerassi, H. Budzikiewicz and D.H. Williams, sets of structure-specific fragmentation rules were established, which enabled organic chemists to interpret the chemical structures of their compounds, even highly complex natural products and drugs. Within a few years, between 1962 and 1964, five books on mass spectrometry of organic compounds were published, three of them by the Djerassi group. In this manner, Carl Djerassi made another significant contribution to medicinal chemistry, besides his research results on optical rotation dispersion and his role in the development of the "pill". Nowdays, mass spectrometry is well established in drug research, for the characterization of new compounds, their structure elucidation and structural confirmation, the identification of drugs and their metabolites in body fluids, and in anti-doping campaigns.

Largely unperceived by medicinal chemists, in the past two decades mass spectrometry developed into a powerful tool in drug discovery, by the detection and analysis of ligand–protein interactions. One of the major breakthroughs to enable such applications was the development of new desorption – ionisation techniques for large-sized, non-volatile molecules, i.e. proteins, RNA, and DNA fragments. The importance of these new tools was honored in 2002, by the Nobel prize in Chemistry for John B. Fenn, Professor at the Virginia Commonwealth University, for his contributions to electrospray ionisation (ESI), and to Koichi Tanaka, an engineer at Shimadzu Corp., Japan, for the development of matrix-assisted laser desorption ionisation (MALDI), sharing the prize with Kurt Wüthrich at ETH Zurich, Switzerland, for his contributions to protein 3D structure elucidation by NMR. In parallel, progress in instrumentation, for better mass (more correctly, mass/charge: m/z) separation and ion detection, and coupling with HPLC separation broadened the field of potential applications.

Whereas mass spectrometry in proteomics was discussed in an earlier volume of this series (Volume 28, M. Hamacher et al. 2006, *Proteomics in Drug Research*, Wiley–VCH, Weinheim), the current monograph focuses on mass spectrometry applications in lead discovery and optimization. As discussed in more detail in the foreword of the volume editors, the chapters provide a comprehensive over-

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view on all current and potential, ''non-classic'' applications of mass spectrometry in various areas of drug research, especially small molecule screening, fragment-based drug discovery, ligand–protein interactions, protein 3D structure characterization, and the study of pharmacokinetics.

The series editors would like to thank Klaus T. Wanner and Georg Höfner, as well as all chapter authors, for compiling and structuring this comprehensive monograph on mass spectrometry techniques. In addition, we want to thank the publisher Wiley–VCH, especially Dr. Frank Weinreich and Renate Dötzer, for their ongoing support of our series ''*Methods and Principles in Medicinal Chemistry*''.

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