Frontiers of Laser Chemical Analysis

Renato Zenobi*

Introduction

I have always been fascinated by how the laser, one of the most powerful tools of modern science, can benefit chemists for initiation of chemical reactions, reaction control, probing of the reaction dynamics, spectroscopic investigation of complex molecules, and for ultradetection in chemical analysis. During my Ph.D. thesis at Stanford University, I had the opportunity to work on a laser mass spectrometry project, in a research group whose activities reach from state-to-state reaction dynamics all the way to laser detection in capillary electrophoresis. The time I spent at Stanford influenced me profoundly. I was involved in collaborations with scientists from many different fields, I became interested in pursuing research projects on my own, and I also saw that an academic career was not as far fetched as it often seems in Europe. Many of my colleagues went on to faculty positions at universities in the United States and elsewhere, and I was encouraged to consider this career path, too. When I was awarded the Alfred Werner Fellowship in 1991, I accepted it because it promised to give me the kind of academic freedom I was hoping for, and I defined it for myself as an ‘externally funded junior faculty position’ in the Swiss system. The Werner Fellowship really gave my career a boost: I started to build up my own research group and to publish independently, successfully attracted research money from several foundations and agencies, and I launched many projects. Some of them still form a basis for my current research at the ETH-Zürich. Below, I briefly explain the areas of research we are currently involved with.

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Introduction

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Scanning Near-Field Optical Microscopy (SNOM)

Optical analysis of surfaces with a spatial resolution below the diffraction limit is possible by scanning a subwavelength (<100 nm) light source in close proximity (<10 nm, i.e., in the optical near field) to an object. Commercial SNOM tips, produced by pipette pulling techniques applied to optical fibers, suffer from poor transmission (∼10⁻⁶). We are using chemically etched tips characterized by a much wider opening angle, a short taper region, and an optical transmission approaching 1%. These tips have allowed fluorescence imaging with <100 nm resolution and excellent signal-to-noise ratios. Very recently, we demonstrated that vibrational spectroscopy with <200 nm spatial resolution is also possible (using surface-enhanced Raman spectroscopy, SERS) [1]. This opens the way to true chemical identification in the submicron range. We apply this to the chemical analysis of molecular surface layers and to materials such as diamond. Pulsed laser radiation can also be transmitted through our SNOM tips. This permits surface modification of polymers and laser-induced desorption of molecular films with ca. 70 nm resolution [2].

Two-Step Laser Mass Spectrometry (L2MS)

Two-Step Laser Mass Spectrometry (L2MS) uses laser-induced thermal desorption from a surface by an infrared laser pulse, followed by gas-phase photoionization by an ultraviolet laser pulse and time-of-flight mass analysis. It is a powerful method for the ultrasensitive and selective mass spectrometric analysis of high molecular weight, nonvolatile, and thermally labile substances. It allows rapid and direct analyses of trace constituents in complex mixtures, and can reach a spatial resolution in the 10⁻⁶ range. We are applying L2MS to a wide range of difficult analytical problems: The analysis of polycyclic aromatic hydrocarbons in kerogens [3] and on environmental aerosol particle surfaces [4], the detection of porphyrin-based photosensitizers for laser cancer therapy in commercial drug formulations [5], and the spatially resolved in-situ analysis of polymer additives [6][7].

Laser-Induced Thermal Desorption (LITD)

The mechanism of intact desorption of thermally labile molecules by Laser-Induced Thermal Desorption (LITD) is still a matter of debate. Using laser spectroscopic methods, we are studying the kinetic and internal energy distributions of test molecules after laser desorption from a variety of substrates. In one study, silylation of silica reduced the internal temperature of laser-desorbed tryptophan by a factor of three, due to the elimination of hydrogen bonding between silanol groups on silica and the adsorbed tryptophan [8]. Results of another study indicate that aniline desorbs from silica with kinetic and internal energies characterized by temperatures below the surface temperature at the time of desorption [9]. However, the latter was extrapolated, not measured simultaneously. We therefore developed a method based on blackbody radiation for noncontact temperature measurement of laser-heated surfaces with <10 ns time resolution [10].

Matrix-Assisted Laser Desorption/Ionization (MALDI)

Matrix-Assisted Laser Desorption/Ionization (MALDI) is one of the powerful recently developed mass spectrometric methods for the analysis of nonvolatile compounds of high and very high molecular weight (up to several 100 000 Da). The ion formation in MALDI is still a poorly understood process. For instance, samples with high electrolyte concentrations such as blood plasma, milk, and other naturally occurring fluids are difficult to analyze by MALDI [11]. The lack of knowledge on ion formation also hinders the rational design of new MALDI matrices. One major thrust of our research is to unravel the MALDI ion formation mechanism. When studying the matrix supression effect in MALDI-MS, we found a new and general mechanism for MALDI ion generation based on recombination of excited matrix species (excitons) [12]. The new model is consistent with available experimental data and also made predictions that were later confirmed experimentally.

Secondly, the problem of efficiently detecting very high-molecular-weight ions is part of our research efforts. Third, we are working on the design of a particle-based two-phase matrices that are reusable and may be employed as a terminating element of a capillary column for direct
Stereoselectivity Control of Free-Radical Reactions Using Lewis Acids

Philippe Renaud*

The development of new methods for the formation of C,C bonds has attracted the interest of synthetic chemists for a long time. An impressive number of stereocontrolled procedures based on ionic and concerted reactions have been developed. During the last 15 years, radical reactions became a useful tool in organic synthesis. For a long period of time, they were considered as essentially non-stereoselective. However, recent developments have completely altered this belief, and subsequent rules were developed to rationalize and predict the stereochemical outcome of cyclization reactions, reactions in rigid systems, and even reactions in acyclic systems [1]. A few years ago, strongly encouraged by the attribution of the Alfred Werner Fellowship, we decided to investigate the use of Lewis acids in order to control the stereoselectivity of radical reactions. Some of our recent results are depicted below.

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Michèle Gerster (left) and Anna-Reine Flah (right) are two graduate students strongly involved in the use of Lewis acids in radical reactions