Multidimensional molecular identification by laser control mass spectrometry

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ABSTRACT

Controlled molecular photofragmentation and ionization achieved with shaped femtosecond laser pulses is coupled with mass spectrometry to achieve a powerful multidimensional tool for fast, accurate, reproducible and quantitative molecular identification. Specific pulse shaping functions are introduced to enhance structure-dependent differences in fragmentation fingerprints. Identification of geometric and structural isomer mixtures is demonstrated. Receiver operational (ROC) curves from our experimental data demonstrate the enhanced reliability that can be achieved by femtosecond laser control mass spectrometry. The potential use of this method for identification of chemicals and explosives with no false alarms is discussed.

Keywords: CBRNE sensing, detection, environment monitoring

1. INTRODUCTION

Mass spectrometry (MS) is one of the most sensitive and reliable methods for the detection of chemicals. However, unlike spectroscopic methods, mass spectrometry provides only the mass to charge ratio for a particular species. This information is not sufficient to make an absolute determination as to the presence of a particular chemical. This is why mass spectrometry has traditionally been paired with other methods (dimensions) of analysis such as gas chromatography GC-MS. Other popular methods to extract additional information have included the use of collisions with electrons or atoms to cause further fragmentation of ions and thus increasing the certainty as to the chemical composition and structure of the precursor ions. These multidimensional methods, known in short as MS^n, have become very popular in particular for the analysis of large molecules such as proteins. Our approach to multidimensional mass spectrometry has been to use a femtosecond laser to induce the molecular ionization. When the femtosecond laser is at its shortest duration, when the pulse is transform limited (TL), the molecular ion usually is the fragment with greatest intensity. We have found that by controlling the spectral phase of the femtosecond laser pulses we are able to create pulses that have a longer duration and this results in further molecular fragmentation. The extent of fragmentation can be easily and reliably controlled. More importantly, every molecule has a specific fragmentation pattern; therefore it is a useful dimension in molecular identification. Here, we will demonstrate that controlled femtosecond laser ionization and fragmentation MS (CFS-MS) is a valuable multidimensional method for the identification of chemicals including isomers.

Modern analytical chemistry relies on multidimensional analysis. In our group we have been developing tools that convert the laser into a multidimensional source for analytical chemistry. In particular, our work focuses on the use of femtosecond lasers. These types of lasers, because of their short pulse duration can achieve extremely high peak intensities (typically 10^{15} W/cm^2); therefore they can easily cause ionization and molecular fragmentation. Unlike traditional pulsed lasers, femtosecond lasers are not monochromatic. This is because the bandwidth of the laser is related to the pulse duration by the uncertainty principle. A typical 35 fs laser pulse, centered at 800 nm, has a bandwidth of 27 nm full-width at half maximum (FWHM). Its entire spectrum spans from 770 to 830 nm. When the phase of all the frequencies within the spectrum of the pulse has the same value (a flat phase), the pulse achieves its shortest duration. These pulses are known as transform limited (TL) pulses. Changes in the spectral phase will inevitably cause pulse broadening. The key for the development of a reliable analytical method using these kinds of lasers is being able to deliver in the instrument femtosecond pulses with precisely defined spectral phase functions.

The means to control the spectral phase of femtosecond laser pulses has been available since the late eighties.[1] These devices are usually called pulse shapers. A femtosecond pulse shaper is similar to a spectrometer. It spreads the pulse into its frequency components. However, instead of having a detector at the point where all the frequencies are spread, the pulse shaper has a mirror that reflects the pulse back out. In front of the retro-reflecting mirror the pulse shaper will typically have a computer controlled liquid crystal panel that can be used to change the phase of individual spectral components. The output pulses carry the phase function they had going into the pulse shaper plus the phase function introduced by the liquid crystal plate. The main challenge in the use of phase shaped pulses has come from the fact that the input pulses usually have some spectral phase distortions that are difficult to measure, and the optics used to stir the pulses towards the target introduce additional unknown phase distortions.

Our research group has introduced a novel method, known as MIIPS, to measure the spectral phase of femtosecond pulses at their target.[2, 3] This method, unlike others that predate it,[4] does not depend on interferometry. Instead it uses reference spectral phase functions and their effect on a nonlinear optical process such as second harmonic generation (SHG) to directly measure the unknown phase distortions of the pulse. Once the unknown phase distortions have been measured, the pulse shaper introduces a negative phase function that cancels the distortions and TL pulses are achieved at the target. This method is similar to noise canceling technology. Being able to start with TL pulses is a critical aspect for robust and reproducible analytical methods. The introduction of additional calibrated phase functions that lengthen the pulse duration and cause additional molecular fragmentation is then achieved through the computer controlled pulse shaper.

2. EXPERIMENTAL

The experiments are performed using a commercially available titanium-sapphire femtosecond laser system capable of producing 0.8 mJ/pulse at a 1 kHz repetition rate. The pulses are 35 fs in duration when compressed using the MIIPS method,[2, 3] and centered at 800 nm. The output of the seed laser (5 nJ, 50 nm full-width at the half maximum) is directed to a folded 2f pulse shaper. The pulse-shaper is based on the dual-mask liquid crystal spatial-light modulator (SLM) where each mask consists of 128 pixels. The SLM is positioned at the Fourier plane of the pulse shaper. Applying different voltages by a computer controlled interface to the individual pixels in the SLM alters the spectral phase of the femtosecond pulses and therefore their shape. After the pulse shaper and amplification, the beam is attenuated to 0.1 mJ/pulse and directed into the vacuum chamber connected to the time-of-flight (TOF) mass spectrometer, or used near the inlet of an atmospheric ion inlet of a TOF mass spectrometer. Samples (simulants of chemical warfare agents) are introduced at a constant pressure in the range of 0.5×10^{-5} to 1×10^{-5} Torr, or used at their ambient vapor pressure. Mass spectra typically averaged 128 laser shots. Typically, a sequence of well-defined spectral phase functions are introduced and the mass spectra are recorded for each of those laser fields. We have constructed a small database that can be used for chemical identification of chemical agent simulants in real time.

3. RESULTS

It has been established that shaped femtosecond pulses can influence the relative yield of fragment ions. In order to determine how different pulses cause difference fragmentation patterns, we carried out an extensive research project in which we evaluated tens of thousands of phases on a total of twenty-five different molecules.[5] We systematically explored different sets of phases for example chirp, sinusoidal functions, random phases, random binary phases, and an entire series of phases representing all possible linear combinations of polynomial functions that can be described with cubic, quartic and quintic frequency dependence. We also tested combinations of phase and amplitude shaping. For our experiments, rather than comparing the ratio between two photoproducts, we decided to plot the observed fragmentation trends as a function of the total ion yield (I_{MS}) for each of the different pulse shaping functions.

One surprising finding was that despite our ability to control molecular fragmentation by orders of magnitude, these changes were not unique to a particular phase function. We found that we could correlate results from very different pulse shaping phase functions provided we matched them by the total (integrated) ion yield I_{MS} normalized to TL pulses. The values for I_{MS} range from one for TL pulses to smaller values as the extent of pulse shaping increases and the pulses get longer in time. For example, we selected very different phases functions (positive chirp, negative chirp, sinusoidal modulation and a binary phase composed of 0 and π values) each of them producing I_{MS} =0.25, and found that they all

caused exactly the same molecular fragmentation pattern.[5] This finding implies that laser controlled fragmentation, as described here, is very robust. This is an essential property when considering an analytical method.

The yield of specific fragment ions exhibits different dependence on pulse shaping for different molecules. Therefore by comparing the change of yield for TL (I_{MS} =1) and shaped pulses we can distinguish one molecule. For example, the relative yield of $C_3H_3^+$ *m/z* 39 decreases for the nitrotoluenes, stays constant for chlorobenzonitrile, and increases for benzene (results not shown). These differences can be used for molecular identification purposes. A full account of these results is published elsewhere.[5, 6]

Here we focus on representative results obtained for molecular isomers. Results for *ortho*-, *meta*- and *para*-nitrotoluene as a function of pulse shaping are shown in figure 1. The lines correspond to results obtained as a function of positive chirp, and the dots correspond to measurements obtained as a function of changing the period of a sinusoidal function. As mentioned earlier, although these two shaping phase functions are absolutely different, when plotting the relative yield of each fragment ions as a function of I_{MS}, we obtain the same changes in the relative yield of all fragments for a given molecule. This observation is confirmed by the agreement between the results represented by the line and those by the dots. Notice that great control over the fragmentation yield (order of magnitude) is easily obtained for either set of phases. Most importantly, we find that the change of relative yield for specific fragment ions is different among different isomers, this observation can be used as a dimension of analysis for MS molecular identification.

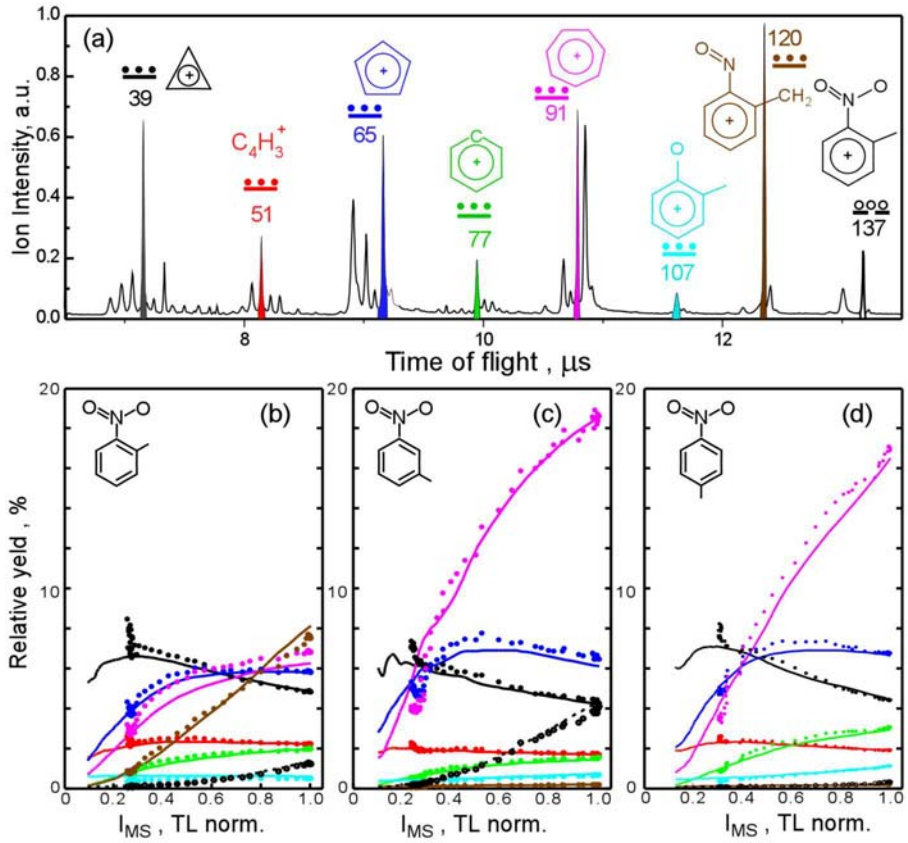

Fig. 1. Experimental results on the laser controlled fragmentation of nitrotoluene isomers. (a) The mass spectrum of *ortho*-nitrotoluene is shown together with the structure of the most common product ions. (b, c, d) Relative yield of the most common product ions for *ortho*-, *meta*- *and para*-nitrotoluene. Results for linear chirp (lines) and changing the period of a sinusoidal function (dots) are compared as a function of I_{MS}. Notice that the changes in the fragmentation pattern coincide for the two very different pulse shaping strategies (lines vs. dots). Changes in the fragment yields as a function of pulse shaping provides a clear distinction between the three isomers.

We use the identification of nitrotoluene isomers as a first example of how pulse shaping can be used for molecular identification. The mass spectrum of *ortho*-nitrotoluene obtained using TL pulses and the assignment of its major ion products is shown in figure 1a. When comparing the fragmentation dependence as a function of pulse shaping, as shown in figures 1b, c and d, we find that the fragmentation patterns are very sensitive to molecular geometry. Here, we see that the differences are not caused by a very specific shaped pulse but by the extent that the fragmentation pattern changes. For *ortho*-nitrotoluene, the product with *m/z* 120 resulting from the reaction between the methyl group and the nitro group is more abundant than the other isomers. This intramolecular hydrogen transfer reaction leads to loss of OH and is favored for TL pulses. Linear chirp can reduce its yield by two orders of magnitude. The ortho hydrogen transfer reaction is favored by ionic states, this is why TL optimizes this reaction pathway.[7] The tropylium ion at *m/z* 91 is a major product for *meta*- and *para*-nitrotoluene, only *ortho*-nitrotoluene produces the tolyl ion at *m/z* 92 with significant abundance. As chirp is increased, the pulse lengthens and multiphoton excitation of intermediate electronic states becomes the dominant ionization-fragmentation process. Differences among the other isomers are more subtle but also identifiable. For example, the molecular ion for *meta*-nitrotoluene has a greater relative yield. The phenylium ion at *m/z* 77 is more likely to be produced from *para*-nitrotoluene. Quantitative analysis for a mixture of *para*- and *meta*-nitrotoluene has been successfully performed by calculating the deviation of the average relative yield of the spectra from the value observed at TL excitation, $\delta \equiv \langle Y - Y_{TL} \rangle$, obtained by a chirp scan.[8] The sign of δ is negative at m/z 107 for both isomers but four times larger for the *para* isomer, which is sufficient to separate *meta*- from *para*-nitrotoluene isomers, and to quantify their concentration in a mixture. The results are shown in Figure 2.

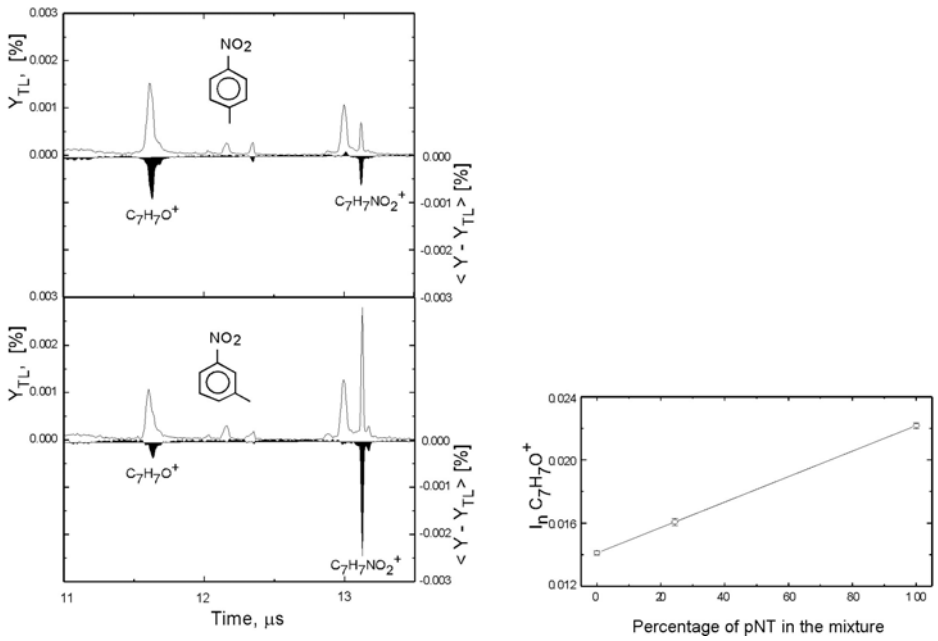

Fig. 2. Portion (m/z > 100) of the mass spectra of *meta*- and *para*-nitrotoluene obtained using transform limited 35 fs pulses (lines - Y_{TL}) with the average deviation δ of the mass spectra (filled areas <Y- Y_{TL}>) observed upon shaping (top two panels). The magnitude of δ can be used as an additional dimension together with m/z for real-time molecular identification. Quantitative analysis of an isomer mixture is shown in the bottom panel. I_n is the integrated value for δ for m/z 107. The three points in the graph represent pure *meta*-, pure *para*-nitrotoluene and a mixture, prepared to be 23.9% by weight of *para*-nitrotoluene in *meta*-nitrotoluene.

Similar experiments have been carried out for several pairs of isomers including xylene, heptene, 4-methyl-2-pentene and cresol.[6] For these experiments we used a set of 10-bit binary phases instead of a chirp scan. Figure 3 shows the results obtained for *ortho* and *para*-xylene with two phases that maximize the difference of their MS spectra. The application of a complex binary phase-shaped pulse resembling BP858 results in a much greater relative yield of the tropylium ion for *para*-xylene compared to that of *ortho*-xylene. The mass spectral fingerprints were normalized to the

molecular ion peak. Quantitative concentration measurements with good statistics and reproducibility were also accomplished for all the isomer mixtures.[6]

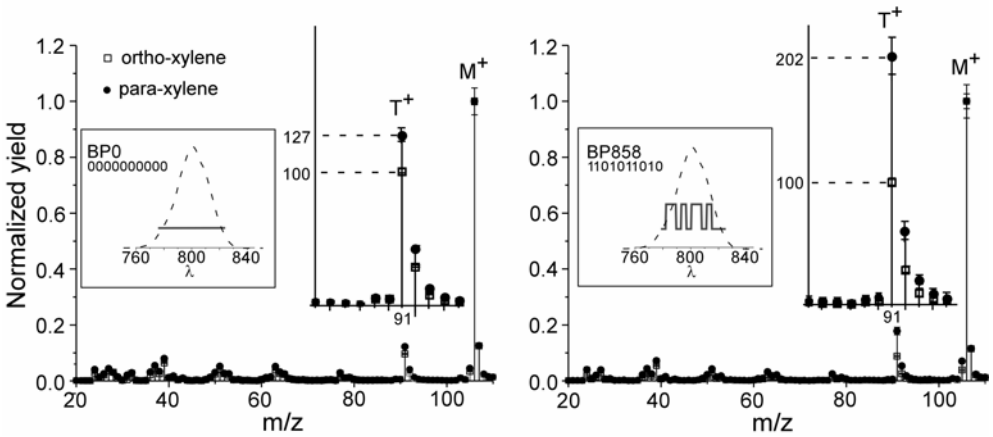

Fig. 3. Mass spectra of the xylene isomers. Left: Results obtained with phase BP0 corresponding to TL laser pulses; the spectral phase of the laser pulse is shown above the mass spectra. Right: Data obtained with laser pulses with binary phase BP858; the phase structure of this pulse is shown above the mass spectra of the isomers. All mass spectra were normalized so that the molecular ion (M^+) intensity equals unity. The region for m/z near 91, corresponding to the tropylium ion (T^+), was amplified to highlight the observed differences. For the BP858 shaped pulses, the relative yield of T^+ for para-xylene is ~2 times greater than that observed for ortho-xylene.

Recently, preliminary results were obtained for ionization and fragmentation with femtosecond laser pulses coupled with atmospheric mass spectrometry. Figure 4 shows the spectra of para-nitrotoluene and trinitrotoluene obtained with this method. For these experiments, the laser causes the fragmentation and ionization under atmospheric conditions. The vapor present is ionized and enters the time-of-flight MS instrument. This patent pending implementation of our experiments will permit the identification of chemical warfare agents, explosives and even medically relevant compounds in ambient air.

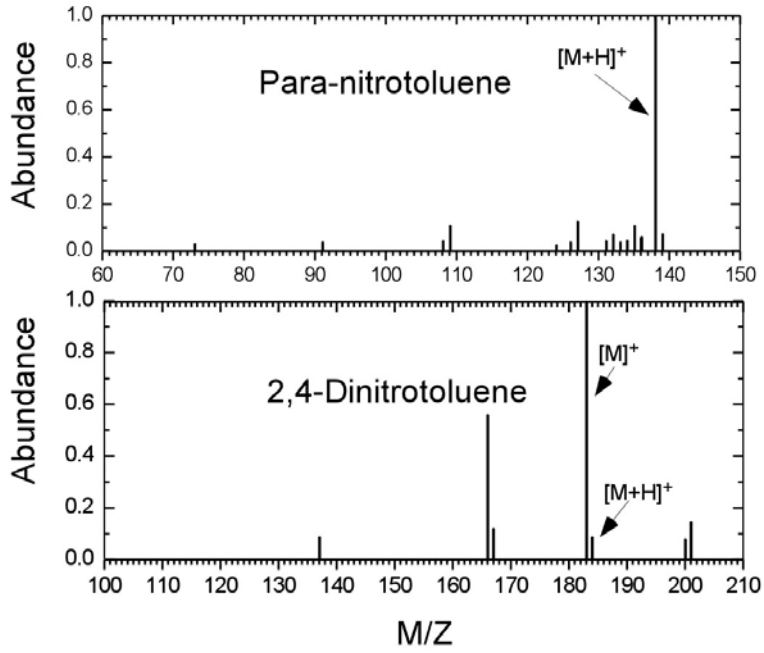

Fig. 4. Mass spectra of para-nitrotoluene and 2,4-dinitrotoluene obtained by ionization and fragmentation with femtosecond laser pulses in atmosphere.

4. CONCLUSION

This brief compilation of recent experiments from our research group demonstrates how phase-shaped femtosecond pulses can be used to control the fragmentation and ionization of molecules. The changes in fragmentation are found to be molecule specific even in the case of molecular isomers. Therefore, we propose that the combination of shaped femtosecond pulses and mass spectrometry can be used for fast, accurate and reproducible qualitative and quantitative identification of chemicals, including stereoisomers. This approach provides a new dimension in MS that is highly sensitive to molecular structure, as required by current biological and environmental applications.

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