Detection of Illicit Drugs by Direct Ablation of Solid Samples

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Abstract

Analysis of illicit drugs rises as an interesting field of work given the high social impact presented by drugs in the modern society. Direct laser ablation of solid compounds enables their analysis without sampling or preparation procedures. For that purpose, an experimental set-up that combines laser ablation with time-of-flight mass spectrometry has been constructed and ulteriorly perform studies on the mass spectra of such drugs as MDMA, commonly known as ecstasy. Analysis of the observed fragmentation pattern in mass spectra may elucidate upon the ablation-induced photofragmentation phenomena produced by ablation, which differs from those previously observed with conventional ionization methods.

Introduction

Direct chemical analysis of solid sample without chemical pretreatment can offer advantage over conventional dissolution techniques used in analysis of real samples such as high pressure liquid chromatography (HPLC) and gas chromatography (GC) coupled with mass spectrometry (MS).[1, 2] Elimination of chemical solvents and wastes, reduced sample handling, and short analysis times are some offered by the benefits of direct solid sampling techniques. Laser ablation has raised considerable interest due to its proven applications in solid sample analysis and consequently different analytical techniques in combination with laser ablation have been developed during the past few decades. Laser-Induced breakdown spectroscopy (LIBS)[3, 4] and laser ablation optical/mass spectrometry with inductively coupled plasma (LA-ICP-AES/MS)[5-10] appear to be amongst the most powerful analytical techniques for nearly non-destructive determination of elements. However, with the growing importance of biomedical and forensic investigations in organic analysis, the emphasis has been shifting towards

detection of ever larger molecules. Hence, devoted laser-based mass spectrometry techniques such as laser microprobe mass analysis (LAMMA)[11-14] and laser desorption/ionization mass spectrometry (LDI-MS)[15-17] have been developed. Among all LDI systems, the matrix assisted laser desorption/ionization (MALDI)[18-20] is the most extended due to its capacity to analyze samples up to 1.5 million of Daltons.[21] However, matrix selection presents itself as a crucial step since matrices are normally too specific and, furthermore, matrix to analyte molar ratio is difficult to adjust correctly.[22, 23] Alternative assistants for LDI, such as metals,[17] surfaces,[24] nanoparticles[25] and polymers,[26] have been developed in order to circumvent the problems with the sample preparation in MALDI.

During the last decade, laser ablation has been successfully combined with Fourier transform microwave techniques (FTMW) to bring thermally unstable biomolecules into gas phase and reveal their most stable structures. Narrowband LA-MB-FTMW[27] and broadband CP-FTMW[28] techniques have overcome the drawback of vaporizing solid samples opening a new window to the high resolution rotational studies. In so doing, the conformational behavior of relevant building blocks such as amino acids,[29] sugars,[30] nucleic acid bases[31] as well as the drugs aspirin[32] and paracetamol[33] could be unveiled.

On the basis of previous experimental setups developed for identifying metallic contaminants[34] and taking advantage of our long experience on laser ablation techniques, an experimental setup that combines laser ablation with time-of-flight mass spectrometry (LA-TOF-MS) has been developed to be dedicated to analyze organic compounds. The instrument configuration is described in the following section and preliminary results on several drugs (such as aspirin and paracetamol) and seized

samples as the illicit drug MDMA (3,4-methylenedioxy-N-methylamphetamine) are reported.

Materials and methods

Experimental set-up

The LA-TOF-MS experimental setup has been developed in-house by using a combination of commercial components. Figure 1 shows a diagram of the overall system. The ionization chamber is a multiport stainless steel vacuum cavity where samples are introduced through port 1. The samples present the shape of a pill, with 8 mm diameter and 5 mm long, and are linked to the holder via heat shrink tube. A gate valve is used to avoid vacuum loses each time a new sample is inserted. The horizontal position of the sample can be adjusted to obtain the best signal. Samples are vertically fixed at halfway point between the TOF extractor and repeller plates. Port 1 is coupled to the time-of-flight (TOF) tube in such a way that its extractor and repeller plates are located in the middle of the chamber. The TOF tube employed is a Jordan type tube of 1 meter long which can operate in reflectron mode (RM Jordan, model D-850). Along the tube, there are several voltage adjustable plates that are adjust to optimize the signal of the samples. All of them are working in continuous mode with the exception of the repeller and extractor plates, which have been modified by two high voltage rapid switches in order to pulse them. The laser beam is introduced inside the ionization chamber though a glass window placed in port 3. This beam is aligned by two external mirrors in such a way that it is equally spaced from both extractor and repeller plates; as such, the laser ablation/ionization is produced perpendicularly to the sample. The laser employed is a Nd:YAG (Quantel Brilliant, model C07.BR) in the third harmonic (λ= 355 nm) with pulse width ~ 5 ns. Its power is adjusted modifying the time delay

between the flash lamp and the Q-S pulse. A single lens (Melles Griot), with a focal distance of 750 mm, which is placed between the above mentioned two mirrors, is employed to focus the laser beam onto the sample. The distance from the lens to the target is tuned by employing a translation stage, which allows to modify the beam spot area in order to obtain a stable signal. The laser spot size is around 0.6 cm^2. Two turbo molecular pumps (Leybold, model TDL RS 458 and TURBOVAC, model 361) connected though port 4 and in the TOF tube are used to maintain the ultra high vacuum required for the experiment. The ionization chamber is generally at 10^{-7} Torr while the reflectron TOF is at 10^{-8} Torr.

The experimental sequence (Figure 2) is controlled by a commercial delay generator (Stanford Research Systems, model DG-645) working at a repetition rate of 10 Hz. Both flash lamp and Q-switch of the laser are externally triggered by the delay generator, being the Q-switch delayed from the flash lamp around 300μs; this time changes in function of the energy that requires the sample to be ionized. A few micro seconds after the Q-switch, the extractor and repeller plates are pulsed during a period that may range from less than a microsecond to 20μs. Delays and pulsed widths are tuned to accomplish the maximum signal of the interested ions. The most common experimental timings are summarized in Table 1. The output signal of the extraction plates is used to trigger the oscilloscope (Agilent model 5464D, 2Gs/s), which digitalized the signal coming from the multichannel plate of the TOF tube. Afterwards, the data is sent to a computer where the analysis and graphing is performed.

Sample preparation

Samples used for the analysis, such as aspirin (m.p.137ºC) or paracetamol (m.p. 171ºC), were purchased to Sigma Aldrich with the exception of MDMA (m.p.100-

110ºC), which is a street sample (not pure), obtained from a seizure by Valladolid division of the Spanish Police Department. This seized sample comes as a fine powder taken from the street. They were used without further purification. These samples were grounded and then introduced into an in-house designed cast and pressed into a hydraulic press at 50 bar in order to form pills with 8 mm diameter and 5 mm long. This procedure has been extensively described in our group reports.[27-33] The flight time data were converted to mass/charge based on the calibrations made with metals samples, (Ag and Cu see Figure 3) which were modeled with the same dimensions as the pills in our laboratory.

Results and Discussion

Prior to the analysis of the illicit drug MDMA, several organic compounds of similar physical characteristics (solids with similar melting points) have been proved by LA-TOF-MS. The pharmacological species paracetamol and aspirin were employed to optimize the experimental conditions and their mass spectra were successfully obtained using this technique (see Figure 4). Both substances exhibit similar fragmentation pattern as those obtained by employing electron impact (EI), a more common ionization source.[35] However, the intensity ratio of the fragments is slightly different. In case of paracetamol, the cleavage between the carbonyl and amino groups (pointed out in Figure 4a) has diminished drastically, leading to observe a major proportion of the parent ion (151u). Likewise, for aspirin, the ratio between the different possible cleavages has changed (see Figure 4b). For EI ionization, the most abundant fragment is by far that corresponding to 120u, with a mininal proportion of the 163u and 138u is minimal, being the latter slightly higher. In contrast, employing LA-TOF-MS, the 120u peak has decreased its intensity and, moreover, the proportion between 163u and 138u

is inverted; in fact, the peak corresponding to 138u does not appear in our mass spectrum.

In light of the results obtained in these initial tests, the analysis of the seized sample MDMA was carried out. This analysis was executed under the same conditions as for previous compounds, with the exception of the laser power whose effects were examined for further optimization. Figure 5 shows several spectra obtained at different fluencies. There, it is remarkable that the value of the energy per pulse might drastically change the aspect of the mass spectrum. At low fluencies, the first signal registered corresponds to a mass/charge of 23 and dominates the mass spectrum even at higher fluencies. This peak presumably corresponds to the Na^+, which is present in most of the commercial organic compounds. Rising in energy, signals of heavier ions become appreciable, including the molecular peak at 194 corresponding to the parent $[MDMA+H]^+$ ion. However, if the energy excesses an optimum value, peaks that correspond to a much higher fragmentation saturate the spectrum (signals around 12 and 24u) while the $[MDMA+H]^+$ disappears. Reaching this energy ranges, laser power is enough to break most of the bonds of the organic molecules that are present in the ablation plume. Thus, for the MDMA analysis, the optimum energy per pulse found is around 6mJ/pulse, which is close to the energy employed for the other organic samples analyzed.

In the MDMA spectrum at 5.7 mJ/pulse (Figure 5b), besides the 194u fragment corresponding to the parent ion plus a proton ($[MDMA+H]^+$), several ions at m/z equal to 30, 42, 58, 122, 105, 135 and 163 can also be attributed to fragments from MDMA (Figure 5). Between the three main possible cleavage sites for ecstasy molecule (Figure 6) β- and γ-cleavages are given in higher proportion according to the almost equal intensity of the fragments m/z=135 and 163, representative of these two cleavages

respectively. Both signals are about three times stronger than the parent ions, which can give us an idea of the fragmentation degree of MDMA under these experimental conditions.

Comparing this LA spectrum with those obtained from more conventional ionization methods, there are clear discrepancies in the relative intensities of the fragments which might indicate differences in the fragmentation procedure. In case of electron impact (EI) ionization, β-cleavage (Figure 5c) dominates the mass spectrum, with negligible intensities of either other fragments or parent ion. This β-cleavage has also higher relevance related to α and γ in MALDI experiments,[36] although, in this case, the photofragmentation degree is minimum; the intensities of the fragment signals are almost exiguous in the spectrum. In contrast to these two ionization methods (EI and MALDI), electrospray ionization (ESI) produces a rupture via γ-cleavage[36] instead of the β-cleavage. On the other hand, as it was mentioned before, both γ- and β-cleavages are produced in almost equal amounts when LA is used to ionize the samples. Thus, LA fragmentation is not produced in exactly the same way as any of them, being more of a combination.

Deeper insight into the MDMA spectrum several reveals that signals with a relative high intensity non assignable to this illicit drug can be distinguished. One should take that the sample analyzed is not a pure sample (estimated purity 70%) into account, otherwise, it was obtained from a seizure made by the Spanish police. Therefore, the presence of other analytes should be expected. By screening in to mass spectrum libraries,[35] it can be observed that several peaks are consistent with the existence of ethylamphetamine, sometimes present together with MDMA as a stimulant. This possible assignment is based on the signals at 72 and 91u and 44 and 119 that might correspond to the pair of ions produced by the break of ethylamphetamine through β-

and δ-cleavages, respectively (Figure 4b). In this case, both types of cleavage have almost the same relevance, similar those in MDMA. However, in the latter, β-type is slightly more intense. The signal at 163u, assigned initially to a γ fragment of MDMA, could also have increased its contribution due to the parent peak of ethylamphetamine shedding some light on the intensity discrepancies between the two peaks produced by γ-cleavage (30u and 163u). Besides these two analytes, no more signals assignable to any other species could be identified in the spectrum.

Conclusions

To the best of our knowledge, this has been the first report of the utilization of conventional laser ablation/ionization TOF-MS spectrometry with the aim of detection the presence of illicit drugs in real samples. Our results have shown the capacity of this technique as a fast diagnostic method with a reduction of the sample processing, which constitute a major advantage, and serves as a foundation for future investigations about the implementation of laser ablation/ionization TOF-MS spectrometry applied to illicit drugs detection. Moreover, it was found that laser ablation produces different fragmentation patterns when compared to most conventional ionization methods (ESI, EI and MALDI). Hence, more work will be necessary to optimize the laser ablation conditions, for instance, using picosecond laser pulses.

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Figure 1. LA-TOF-MS instrument.

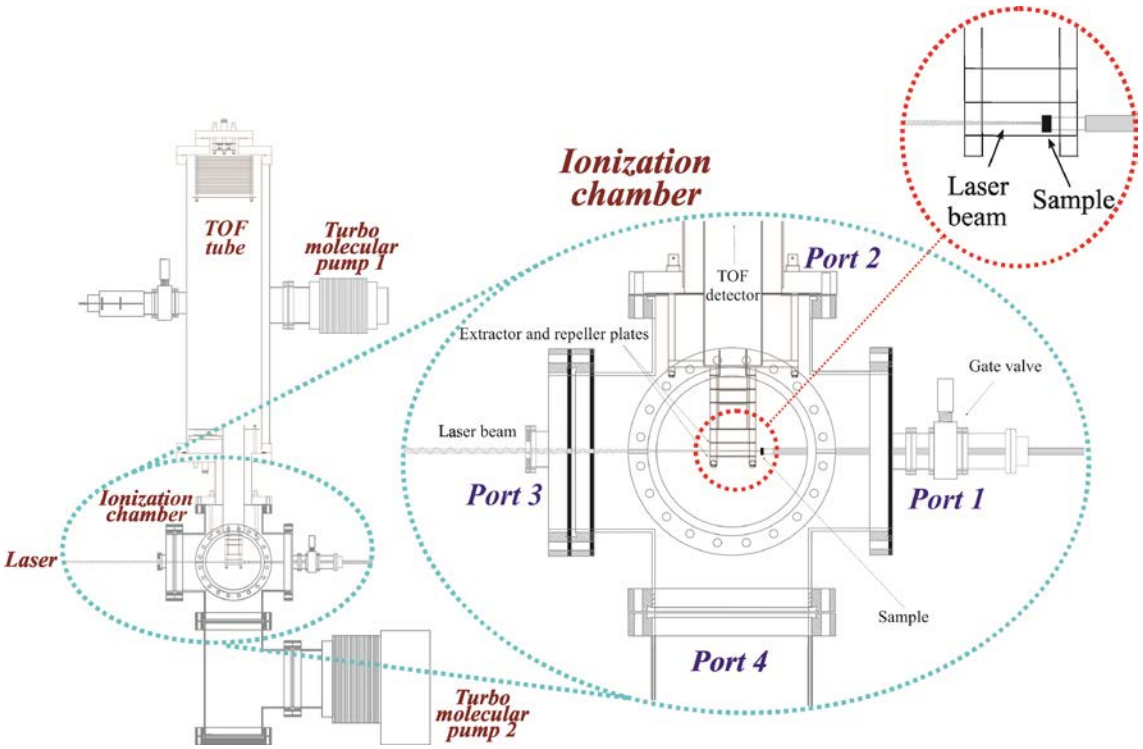


Figure 2. Operating sequence of LA-TOF-MS controlled by pulse delay generator.

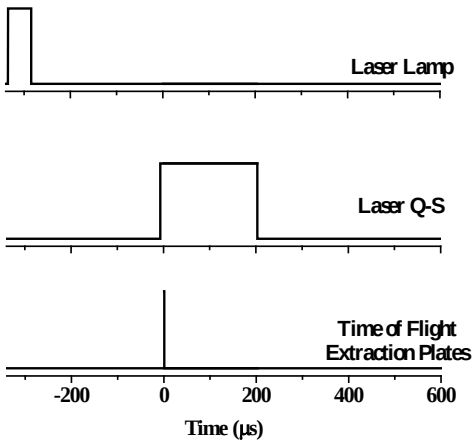


Table 1. Summary of the operating parameters of the LA-TOF-MS system

Laser	
Wavelengh	355nm
Pulse width	10 ns
Energy/pulse	0.5 – 15mJ
Rep rate	10Hz
Spot size	0.6 cm^2
Time of Flight	
Preassure	~10^{-7} Torr
Extraction plate	~ 2800 V
Repelling plate	~ 3250 V
Reflection plate 1	~ 1800 V
Reflection plate 2	~ 4000V
Deflection plates	~ 0 V
Detection plate	~ -4000V
Pulse delay generator	
Delay Flash lamps / Q-switch	300 – 350 µs
Delay Q-switch / Extraction plates	1-15 µs
Pulse width of extraction plates	0.5 - 5 µs

Figure 3. Mass spectra of some metals obtained from LA-TOF-MS instrument.

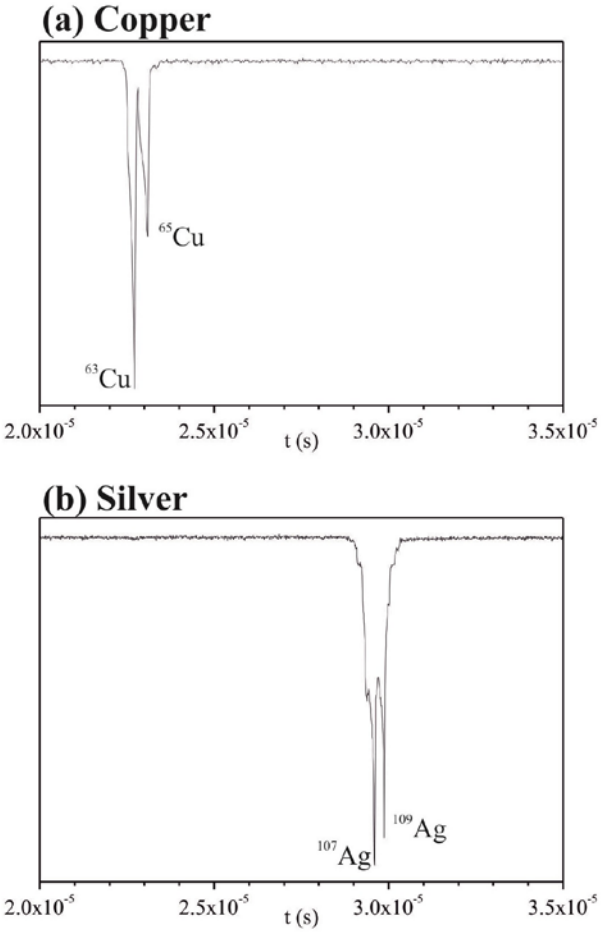


Figure 4. Mass spectra of paracetamol (151u) and aspirin (180u) obtained from LA-TOF-MS instrument.

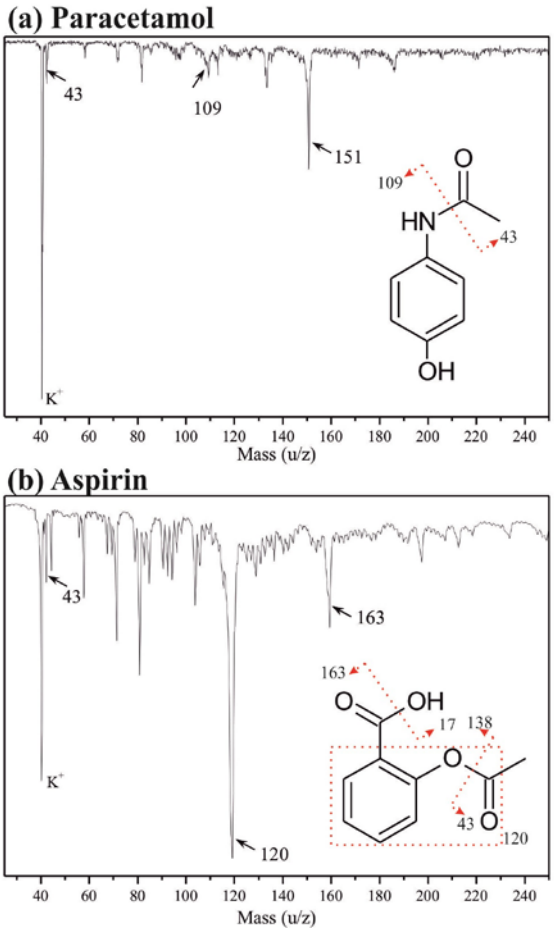


Figure 5. (a) Mass spectra of MDMA at different fluencies. (b) Mass spectrum of MDMA at 5.7mJ per pulse amplified. (c) α-, β-, and γ-cleavages of MDMA.

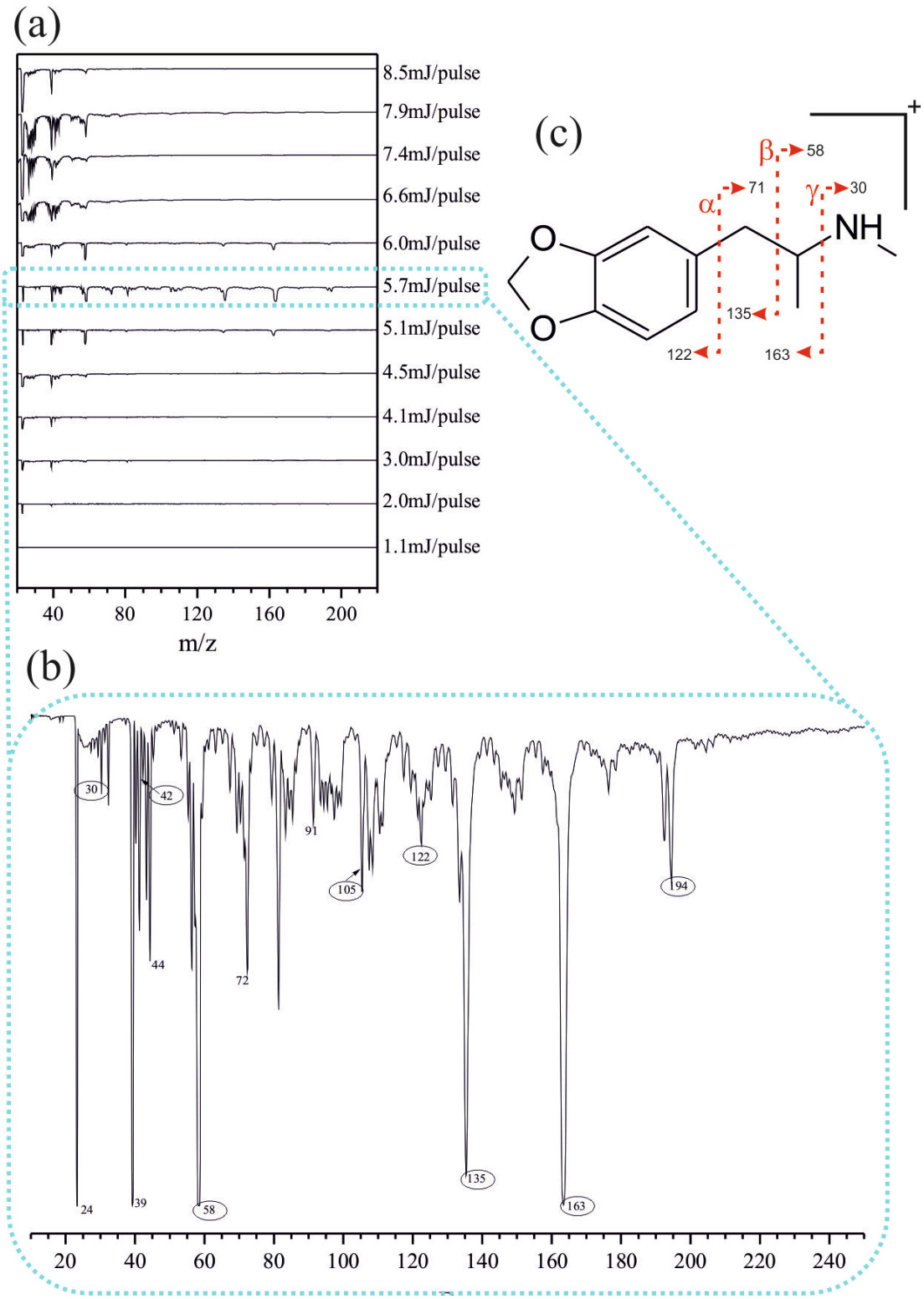
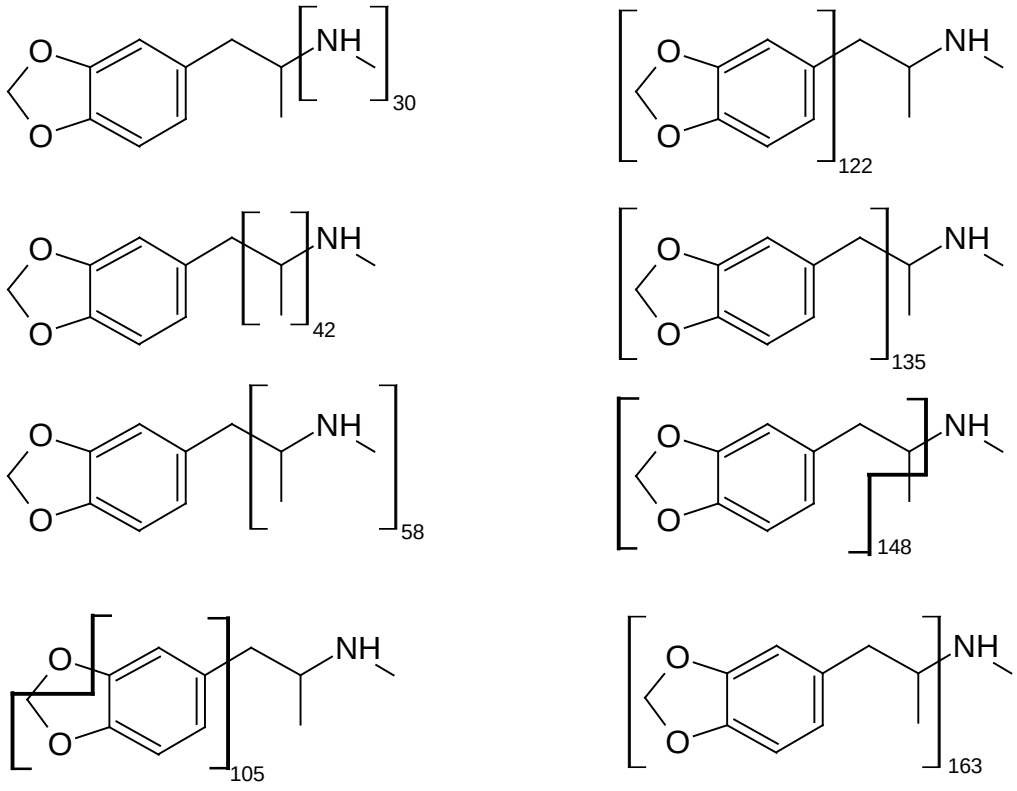


Figure 5. Fragments of MDMA identified in the mass spectrum.



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