Development of a LC-QIT-TOF mass spectrometer capable of high mass accuracy and stability.

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Overview

In this paper we report the factors that improved mass accuracy and mass stability of a LCMS-IT-TOF system.

The effect of the cooling gas on performance was studied. Mass resolution was tested with Helium and Argon and the results were compared.

With Argon cooling , the instrument showed better mass resolution compared with conventional Helium cooling .Also, pulsed Argon introduced into the ion trap enhanced CID efficiency.

The time of flight mass analyzer was thermally regulated to avoid expansion of the flight tube and drift of the output voltage of the power supplies.

This instrumental configuration has led to high resolution (>10,000) and high mass accuracy (< 5 ppm, external calibration) being routinely achieved.

Introduction

A quadrupole ion trap coupled to a time of flight mass analyzer potentially has the ability to provide high resolution and high accuracy mass spectra in MS and MS^n modes. Technology developed for a high performance QIT-TOF configuration with a MALDI source was reported previously by Tanaka et al. [1]. Based on their technology, a QIT-TOF with an ESI source has been developed using novel ion introduction optics [2]. Instrument performance characteristics have now been extensively investigated in regards to mass accuracy and stability. This paper describes the result of this study.

Methods

For the conventional ion trap instrument, ions are continuously introduced into the ion trap. In this case, only the ions that get into the ion trap in a limited ring RF phase can be trapped. In other phases, ions are either overly accelerated or repelled by the ring RF voltage and are lost. In the case of the LCMS-IT-TOF (Shimadzu Corporation), the continuous flow of ions generated by ESI were focused into an octopole, which was part-coated with a resistive material at the exit end. An electric potential gradient along the ion beam axis line was formed in this resistive region. In combination with an ion stopping voltage on the electrode adjacent to the octopole, this formed a potential well in which ions were accumulated. The ions in this region were then released into the ion trap by switching the stopping voltage to an accelerating voltage. Thus, the continuous ion beam from the source was converted into a pulsed flow of ions. The ring RF voltage was rapidly activated when most of the pulsed ions where inside the ion trap, trapping the ions with very high efficiency. For ion ejection, a bipolar DC voltage between the two end cap electrodes was rapidly applied whilst simultaneously turning off the ring RF.
The factors affecting mass accuracy and mass stability were investigated to optimise performance. The effect of the cooling gas on performance was studied. Argon cooling gas was used in place of the commonly used Helium. Mass resolution was tested with both gases and the results were compared. Other factors that influence the mass resolution and mass accuracy were also investigated.

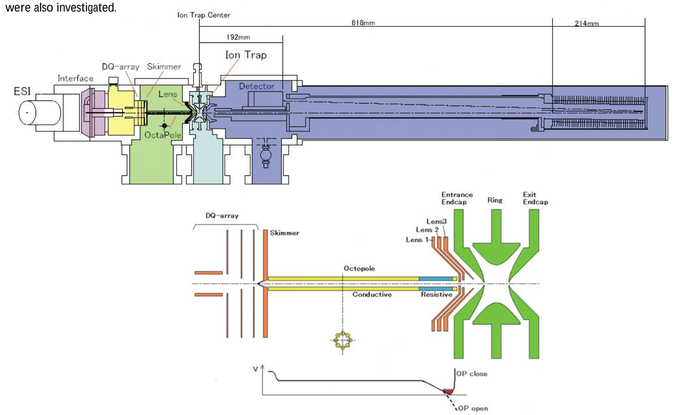

Figure *1*. Schematic of the LCMS-IT-TOF MS configuration & the ion introduction optics

References
[1] Koichi Tanaka et al. Proc. 47th ASMS Conf. Mass Spectrometry and Allied Topics, Dallas,TX,1999.
[2] Kozo Miseki et al. Proc. 51st ASMS Conf. Mass Spectrometry and Allied Topics, Montreal, Canada, 2003.
[3] Danellet al. J. Am. Soc. Mass Spectrom. 2003, 14, 1099-1109.

Results

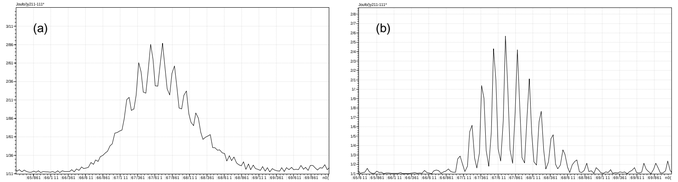

Figure 2.The mass spectra of Bovine Insulin (m/z 956, $[M+6H]^{6+}$) with (a) Helium cooling and (b) Argon cooling

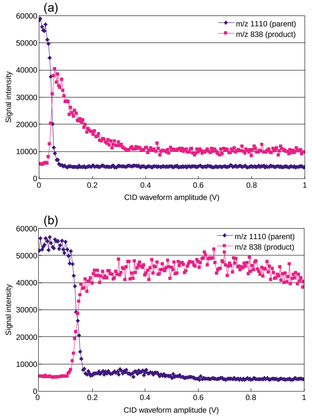

Figure 3. CID efficiency
(a) without pulsed Argon (b) with pulsed Argon

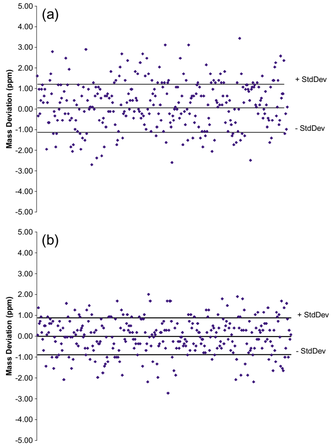

Figure 4. Mass stability over 24h
(a) External cal., (b) Internal cal.

Results and Discussion

Experimental results of Argon cooling showed better resolution in comparison to Helium cooling, especially in the high mass region. Figure 2 shows the mass spectra of bovine insulin (m/z 956, $[M+6H]^{6+}$) using either (a) He (4.5×10^{-2}Pa corrected) or (b) Argon (7.5×10^{-3}Pa corrected) as the cooling gas. The spectrum of He cooling showed poor mass resolution and was not fully resolved. However, by using Argon, resolution of >12,000 was achieved. The higher damping efficiency of Argon better localized the trapped ions and the initial space and energy distribution for the TOF analyzer was reduced. This lead to higher mass resolution and accuracy. Additionally, the amount of Argon required for the best sensitivity was less than that of Helium, resulting in a decrease in the collision frequency when the ions were ejected to the TOF analyzer. When Argon is used as the cooling gas with ion trap mass analyzers, it has been reported that the mass resolution was degraded [3]. In the case of the mass selective instability scan, ions experience a high q value just before ion ejection and at that time, energetic collisions with Argon can degrade the performanceof the ion trap mass analyzer. In the case of the LCMS-IT-TOF, the mass spectrum is acquired by simultaneously ejecting all the ions to the TOF mass analyzer, which means that the q value does not have to be increased. The configuration of the LCMS-IT-TOF does not suffer from the restriction that the ion trap mass analyzer encounters and can take full advantage of using Argon cooling.

The Argon not only enhances the cooling efficiency, but also enhances the CID efficiency [3]. The LCMS-IT-TOF system is equipped with a pulse gas valve, which injects a short pulse of Argon immediately prior to the CID waveform being applied. This further enhances the CID efficiency. The pulsed Argon works as to prevent the parent ions from being lost before fragmentation takes place. Figure 3 shows the variation of parent ion (m/z1110) and product ion (m/z 838) intensity of NaTFA sample as a function of CID waveform power. Without the use of pulsed Argon, the intensity of the product ion decreases as the CID waveform power increases. That is because the parent ions are lost without being fragmented. With the pulsed Argon, the intensity of the product ion does not decrease even with a higher power CID waveform. This made it possible to avoid adjusting the CID waveform power depending on the m/z value of the parent ion, as is necessary with a conventional ion trap. This is also true when a low q value for CID is used, which means that the low mass cut off can be set at a lower value without affecting the CID efficiency, thereby making it possible to observe the lower m/z fragment ions. Figure 5 shows the MSn acquisition of a NaTFAsample. The highly efficient CID makes it possible to acquire MS^{10} data without losing product ion intensity.

One of the main factors that affected the mass stability was the thermal expansion of the flight tube and the fluctuation of output voltage of high voltage power supplies connected to the flight tube. To address this, the temperature of the flight tube, the high voltage power supplies for the flight tube and the control circuitry was regulated to within +/-0.3 degrees C. Figure 4 shows long term mass stability of NaTFA(m/z928) with external and internal calibration. The stability of this system has been shown to be within 3 ppm over 24 hours.

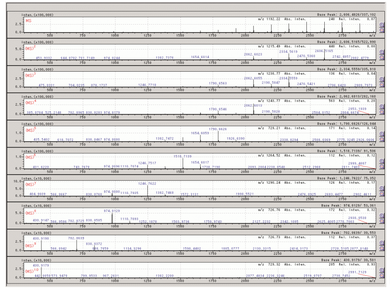

Figure 5. MS^{10}using NaTFA sample

Conclusions

- The higher damping efficiency of Argon better localized the trapped ions and contributed to higher mass resolution and accuracy.
- The use of Argon as a pulse gas injection further enhanced the efficiency of CID.
- The flight tube and power supplies were thermally regulated, leading to mass calibration stability of 3 ppm over 24 hours.
- This instrumental configuration has led to high resolution (>10,000) and high mass accuracy (< 5 ppm, external calibration) being routinely achieved.