



Characterization of Ion-Molecule Reactions within Quadrupole Ion Trap Mass Analyzers by Chemical Modification of the Collision Gas



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Introduction

Motivation

- Increasing the mean and the maximum charge state of large molecular ions – called *supercharging* – is desirable in modern ESI-MS
- Two different approaches are known
 - addition of "supercharging agents" to the sprayed analyte solution
 - addition of solvent vapors ("chemical modifiers") to the matrix gas of the ion source
- The exposure of electrospray droplets to chemical modifiers tends to produce inconsistent results in the literature

Hypotheses

- Ion-solvent interactions are crucial in the competitive situation between charge depletion and charge conservation
- Characterization of the ion-solvent reactions leads to a better understanding of the observed results

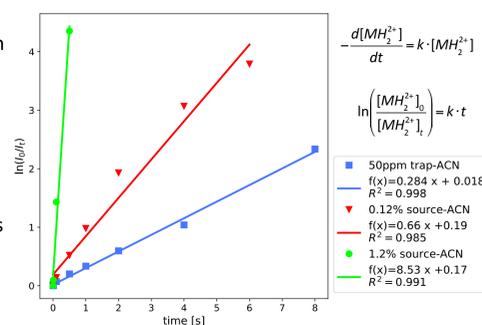
Experimental implementation

- Addition of acetonitrile (ACN) to the helium collision gas within the trap
- Comprehensive study of the results of the chemical modification

Reaction Kinetics

The concentration-time-profile of the doubly protonated 1,9-diaminononane, MH_2^{2+} , was analyzed to determine the reaction order. On the assumption that the ions only react with neutral molecules, which are present at constant and high mixing ratios in comparison to the ion population, pseudo-first-order kinetics is assumed. The linearized plots show that the experimental data support this assumption. Increasing the amount of ACN results in increasing values for the pseudo-first order reaction rate constant k . Unfortunately, the resulting ACN mixing ratio in the collision gas is not known when ACN is added to the ion source. Plotting the slopes of the source-ACN measurements, the increase of one magnitude in concentration is reproduced in the values for k .

For an accurate determination of the rate constants and the actual ACN mixing ratios present in the trap, more experiments are required. In addition, simulations of ion trajectories considering collisions with background gas particles and chemical reactions are planned.



Methods

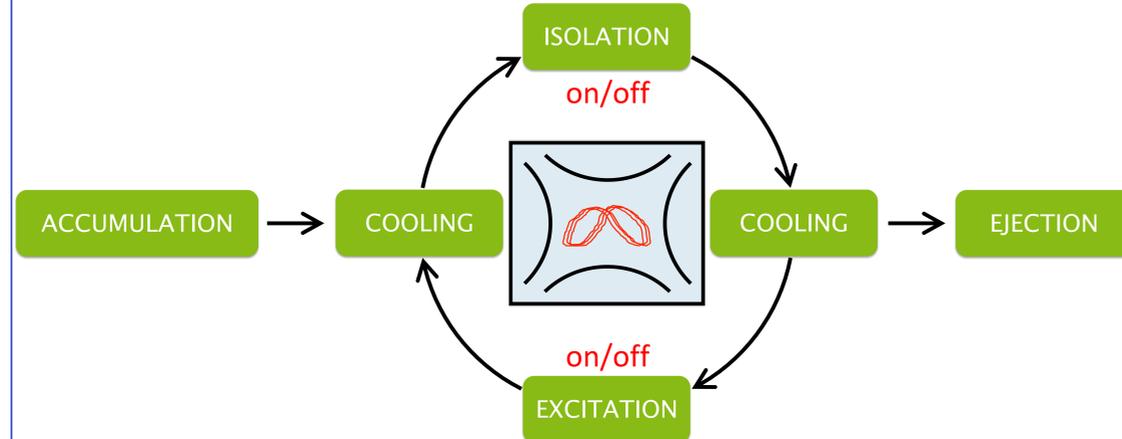
MS: esquire3000 HCT, esquire6000 (Bruker Daltonics, Bremen, Germany)

Ion Source: Custom nano Electro Spray Ionization (nESI) Source [1];

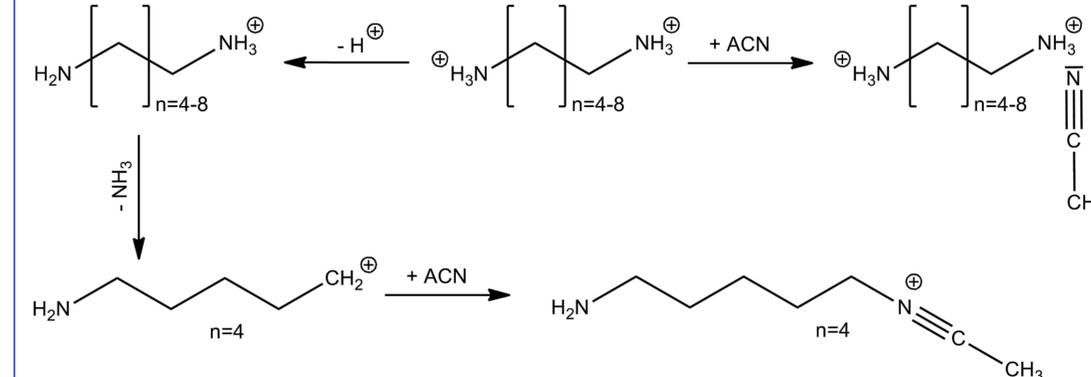
Gas Supply: Boil-off nitrogen (Linde Gases Division, Pullach, Germany), all gas flows are controlled by mass flow controllers (MKS Instruments, Germany)

Chemicals: Chemicals were purchased from Sigma Aldrich, Germany, and used without further purification. Analytes: 1,9-diaminononane, 1,5-diaminopentane, modifiers: methanol (MeOH), acetonitrile (ACN) and deuterated acetonitrile (ACN-d3)

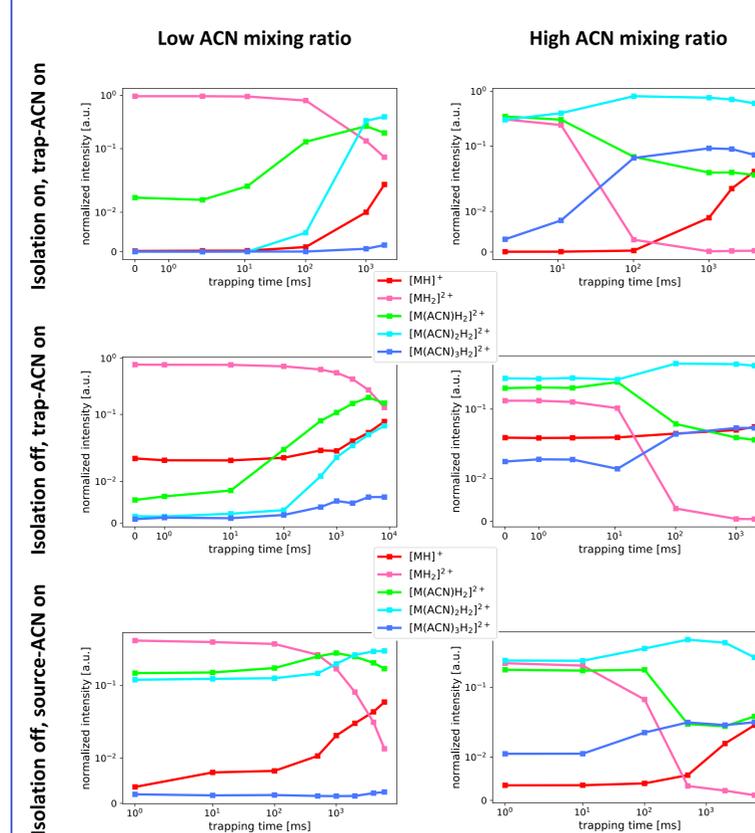
Measurement Procedure



Reaction Scheme



Variation of the Cooling Time



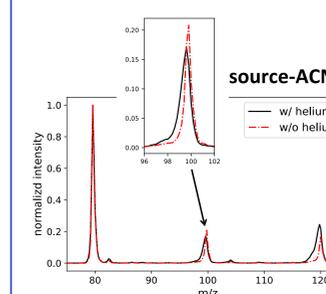
To observe ion-molecule reactions, ions are stored up to 20 seconds in the trap. No ion loss is observed during cooling, the total ion current (TIC) remains constant. The ion population remains unchanged as long as the collision gas (helium) is not chemically modified. When neutral ACN is present in the trap, 1,9-diaminononane (singly protonated MH^+ and doubly protonated MH_2^{2+}) undergo reactions (see reaction scheme). ACN is introduced either directly to the trap via the helium collision gas line (**trapACN**) or to the ion source via the nitrogen line (**sourceACN**).

Left, top: After ion accumulation, the MH_2^{2+} is isolated, which is clustered with ACN resulting in $MH_2(ACN)_n^{2+}$, $n=1-3$. The mean cluster size depends on the reaction time and the ACN mixing ratio. At a higher trapACN mixing ratios the equilibrium is reached after approximately one second. In addition to the clustering/decustering reactions, deprotonation of MH_2^{2+} to yield MH^+ is observed – irreversibly and with a significantly smaller reaction rate.

Left, center: Starting with both species, MH^+ and MH_2^{2+} , does not change the reaction system.

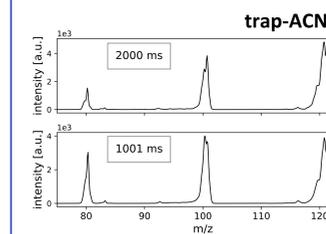
Left, bottom: The addition of high amounts (mixing ratio in the percentage range) of ACN to the ion source entails that neutral ACN is also present in the ion trap. Due to this fact the mean cluster size with which the ions enter the trap increases during the trapping time.

Chemical Mass Shift: Peak Width and Asymmetry



Above: In case of the cluster species peak fronting is observed. Decreasing the collision rate by switching off the helium buffer gas improves the peak width and symmetry. Dissociation of the fragile ions is inhibited. The shape of the stable MH_2^{2+} signal remains unchanged.

Right: By decreasing the scan rate the ions remain longer in the excitation field. Thus, the extent of dissociation is larger when they are less stable. The difference in peak widths between less stable ions and more stable ions becomes larger [2]. In contrast, decreasing the scan rate also results in better resolution and peak symmetry, especially for clustered ions, as shown in the mass spectrum on the right.



Isolation of MH_2^{2+} yields symmetric and intense signals whereas the isolation of $MH_2(ACN)_n^{2+}$ does not generate any proper spectrum.

Left: In the presence of ACN, isolation of MH_2^{2+} and subsequent cooling for several seconds generates cluster species. In contrast to the high capacity (HCT) esquire trap the regular esquire trap shows *peak splitting* at low helium pressures. Peak splitting is often caused by nonlinear field components and removed by elastic collisions with the buffer gas or by trap geometry optimization (\rightarrow HCT) [3].

Literature

- M. Thinius, M. Langner, H. Kersten, T. Benter, Impact of chemical modifiers on the cluster chemistry during electrospray ionization, *Proceedings of the 63th ASMS Conference on Mass Spectrometry and Allied Topics*, San Antonio, TX, USA (2016)
- J. McClellan, J. Murphy, J. Mulholland, R. Yost, Effects of fragile ions on mass resolution and on isolation for tandem mass spectrometry in the quadrupole ion trap mass spectrometer, *Anal. Chem.*, 74 (2002), 411
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Summary / Outlook

- Clustering with the chemical modifier ACN is described as equilibrium reaction system
- Decay of MH_2^{2+} is described as first-order reaction
- Ions clustered with ACN are fragile chemical species
- ACN conserves the charge of doubly protonated species
- Simultaneous addition of sourceACN and deuterated trapACN to study the individual clustering/decustering reaction steps
- Further studies of the chemical shift and the ion stability
- Use of other chemical modifiers

Acknowledgement

Financial support is gratefully acknowledged:

- Bruker Daltonics, Bremen, Germany
- iGenTraX UG, Haan, Germany