

Referee #1

1. **Page 1, lines 20–21:** I recommend changing the unit from ppq to molecules cm^{-3} , or showing both, when possible. A major motivation for achieving such low LODs is to probe nucleation events (as authors mentioned), where reporting in molecules cm^{-3} (e.g., 2.5×10^4 molecules cm^{-3}) is more intuitive and widely used than 1 ppq. That said, using ppq occasionally is fine for readers from the gas-phase or trace gas community. I particularly appreciated Figure 2 and line 237, where both units are shown, this is a good practice and should be applied more consistently.

Reply

We agree that molecules or ions cm^{-3} is a more intuitive unit and that it should be used more consistently throughout the paper. We have made the necessary changes throughout the manuscript, often providing both units for the better understanding.

2. **Scientific notation and formatting:** Please check the formatting of numbers throughout the manuscript:
 - Page 1, line 41: change “10.000” to “10,000” (use a comma for thousands, not a dot)
 - Page 2, line 57: change “10-5%” to correct scientific notation, e.g., “ 10^{-7} ”

Reply

We appreciate the comment of the reviewer here. We have changed the formatting to scientific notation.

3. **Define abbreviations at first use.** Several abbreviations are used without definition:
 - Page 2, line 64: Define “Ts” here rather than in line 65.
 - Page 2, line 66: Clarify what “ioniAPi-TOF-MS” means, is this a typo?
 - Page 2, line 98: Define “DC” at first mention.
 - Page 4, line 147: Define “THAB”.
 - Page 5, line 159: Replace the first “TPAI” with “TMAI”, possibly a typo.

Reply

- The ioniAPi-TOF-MS is the APi-TOF-MS produced by Ionicon Analytik GmbH. We have now clarified this by mentioning the manufacturer in brackets
- Other proposed changes were made.

4. **Page 3, line 108:** Remove “Fig. 1” after “Gate 1”, it is redundant.

Reply

The correction has been made.

5. **Page 5, lines 165–166:** Please rephrase this sentence. The LOD is not typically defined as the signal from a single ion striking the detector. Rather, it is defined as the lowest signal that can be reliably distinguished from noise. Your explanation in Supplementary Section S3 is much clearer and more accurate: “The lowest possible signal that the TOF detector of the APi-TOF-MS can measure is that of a single ion striking the detector (S_{aon}).”

Reply

We agree with the reviewer here. The correction has been made.

6. **Figure 4 and m/z dependence:** Figure 4 presents ion transmission for a specific accumulation time (T_a). The authors mention extracting ions at three consecutive time points per spectrum to minimize mass bias during accumulation. I wonder whether the **trapping efficiency also varies with m/z**, for example, low-m/z ions are unstable due to higher kinetic energy or mobility. Could this be dependent on T_a as well? Comparing transmission curves for different T_a could be insightful and would strengthen the discussion on mass bias.

Reply

The reviewer correctly points out that the trapping efficiency over time in the octapole ion trap potentially varies with m/z. We have not investigated this effect in the current work, but we plan to do so in the near future. A sentence highlighting this point has been added in the updated version of the manuscript.

7. **Page 9, line 312:** The authors reference results from Density Functional Theory (DFT) calculations, but note that they are not shown. If possible, please provide a reference to these calculations or supplementary material for readers who may wish to explore them further.

Reply

We thank the reviewer for this point. We have added a new section in the supplement (Section S.5) providing a description of the simulations performed to test the stability of THAB and TPAI. Please note that adding this analysis requires the addition of a new co-author, Dr. Somnath Bhowmick.

Referee #2

1. Line 66: typo? What do you mean by ioniAPi-TOF-MS

Reply

The ioniAPi-TOF-MS is the APi-TOF-MS produced by Ionicon Analytik GmbH. We have now clarified this by mentioning the manufacturer in brackets.

2. You should ensure that each abbreviation is defined before it appears for the first time. For example, in line 87, “ESI” is introduced before its meaning is explained, which you explain them in the following section. In Figure 6, the abbreviations “TPAI” and “THAB” are used in the caption, but they are not consistent with those shown in the figure itself.

Reply

We thank the reviewer for pointing this out. We have made necessary changes throughout the entire manuscript.

3. In Table 1, some units are presented alongside the input parameters, while others are placed with the values. Please make the unit placement consistent throughout the table.

Reply

We have made necessary corrections, improving the consistency on how we refer to the units through the manuscript.

4. In general, did you describe what kind of solutions that you made for ESI to generate the ions shown in Table 2? I did not find them. I think it is better to include this information in paper.

Reply

We agree with the suggestion of the referee to add the details on the ESI solutions. We have added a relevant part in section 2.2.

5. In line 147, line 256: How did you operate DMS to select single ions with different mass to charge ratio? You only mentioned the parameters to select the THAB monomer, how about others that you listed in Table 1.

Reply

We understand that the reviewer here wanted to write DMA instead of DMS, and that parameters for the THAB monomer are the ones provided in Table 2 and not Table 1.

The parameters to select monomers and dimers other than THAB was only the potential difference between the two plates of the DMA electrodes. We have modified the text accordingly for clarification.

6. Line 198 and 200: Water molecules can also have an effect on the binding energies of ion-molecular clusters, which can help to stabilize the ion-molecular clusters. Please have a look at the paper 'Computational Comparison of Different Reagent Ions in the Chemical Ionization of Oxidized Multifunctional Compounds'.

Reply

The reviewer brings up an interesting point, that ion-molecular clusters can be stabilized by binding to water molecules. Since water is presumably absent in our measurements (the electrospray solutions we prepared in acetonitrile), we expect that the effect of water on the binding is negligible in this study. However, for ambient measurement, indeed the stabilization by water molecules can play an important role, where fragmentation of these water-bound clusters is possibly reached at far lower energies than seen in this study. We have included the reference and pointed out, that the presence of water can have a significant effect on binding energies.

7. In section 3.2. How did you operate the system to define the transmission? What kind of ions with what mass that you used to define the transmission? Do you mean all the ions that you listed in table 2?

This paragraph has now been updated, and addresses the point of the reviewer here clarifying the setting of the API-TOF-MS during the transmission measurements.

8. Line 315: Is there any reference here?

Reply

Given that referee #1 made a similar comment, we have added chapter S.5 in the supplement providing an in-depth explanation on the simulations performed to test the stability of THAB and TPAI to the supplement.

9. Line 315-319: What would you obtain in mass spectrum if the dimer ions dissociate? If I understand correctly, I would say, it should be one neutral molecule and one ion-molecule cluster. That means it should not be the neutral monomer in your figure 6. For example, the possible combination should be (C₁₂H₂₈N)₂I⁻, (C₁₂H₂₈N)I⁻ and (C₇H₁₆N)I⁻ in panel a, but not (C₁₂H₂₈N)₂I⁻, C₁₂H₂₈N and C₇H₁₆N. The same case for panel b.

Reply

We have specified the chemical formulas of possible products of the dissociation of the THAB and TPAI dimers in Figure S-8 in the supplement.

Based on comment 2 of the reviewer, we have chosen to change the terminology in the legend to "TPAI" and "THAB" monomer/dimer, making the chemical formulas redundant in Fig. 6.