Ammonium-Adduct Chemical Ionization Mass Spectrometry (NH_4^+ CI-MS): Selective, Soft Ionization of VOCs

TOFWERK's Vocus chemical ionization TOF mass spectrometers can be operated with multiple reagent ion chemistries to target different classes of compounds. One especially powerful technique uses ammonium-adduct ion-molecule chemistry for selective, soft ionization of volatile organic compounds (VOCs).

Basic Principles

A DC plasma ion source generates high concentrations of NH_4^+ reagent ions, which are mixed with target analyte molecules in the Vocus ion-molecule reaction chamber (IMR). Ligand switching reactions result in analyte-NH_4^+ adducts without fragmentation (Figure 1). The bright ion source and efficient Vocus reactor are coupled to a TOF mass analyzer, yielding extremely low detection limits for even sub-second averaging times.

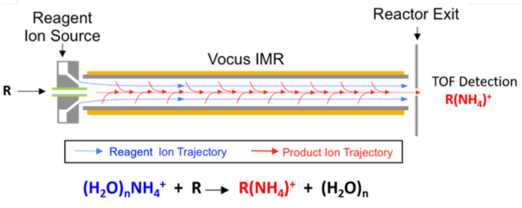

Figure 1 *NH_4^+ reagent ions are generated in a plasma source and* ionize analyte molecules in the Vocus reactor.

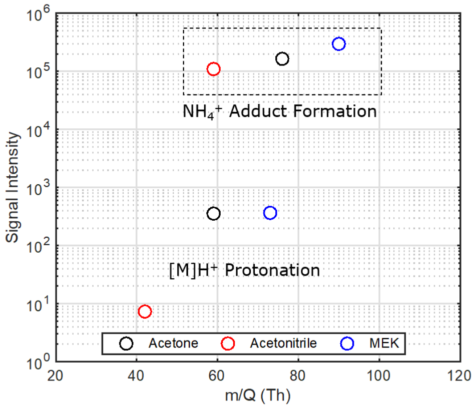

Figure 2 *Efficient ammonium-adduct formation creates a clean mass spectrum. Here spurious proton-transfer reactions involving the target analytes acetone, acetonitrile, and methyl ethyl ketone account for less than 1% of observed signals.*

Ensuring that only one type of ion-molecular reaction occurs in the IMR is important for making the spectrum easily interpretable. Adducts form efficiently in the Vocus IMR under low-energy collision conditions, and spurious ion-molecule reactions (e.g., proton transfer) that could complicate the mass spectrum are minimized (Figure 2).

Operating the IMR at low pressures improves the ability to control the energy of reagent ions and subsequent ionization processes impacting water vapor dependence, absolute sensitivity, and other characteristics. Electrostatic fields across the length of the reactor help control cluster distribution, and water vapor is added from the ion source to buffer against ambient water vapor changes. As when the Vocus CI mass spectrometer is used for proton transfer reaction ionization (PTR, H_3O^+ reagent ions), instrument response has negligible dependence on ambient humidity, greatly reducing instrument sensitivity to changes in environmental conditions (Figure 3).

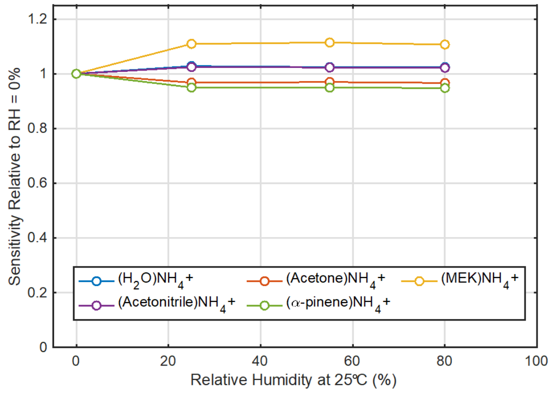

Figure 3 *Vocus NH_4^+ CIMS sensitivities remain constant across a wide range of ambient humidity. The data points for $(H_2O)NH_4^+$ and (Acetonitrile)NH_4^+ overlap.*

The same Vocus ion source and IMR are used for NH_4^+ adduct and PTR mass spectrometry, allowing fast, real-time switching between NH_4^+, H_3O^+ and other reagent ions. As shown in Figure 4, the switching is automated, reproducible and stable.

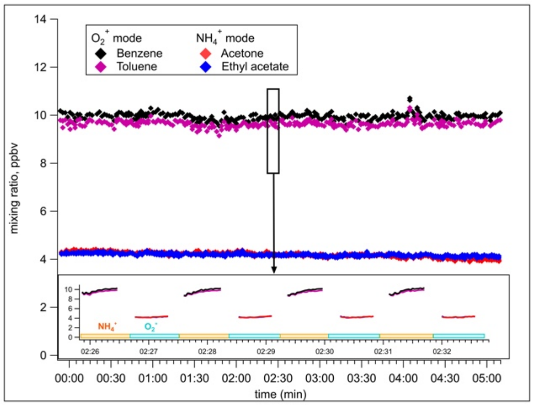

Figure 4 *Automated switching between NH_4^+ and O_2^+ reagent ions. A fixed calibration gas was measured for several hours. The reagent ion was switched every minute between NH_4^+ and O_2^+ reagent ions, allowing the real-time measurement of oxygenated species that typically fragment in conventional PTR-MS, as well as standard species such as BTX and acetone. The full time-series shows the average of one-minute data, and the insert shows 1-second data for a select period.*

Benefits of NH_4^+ Adduct Chemical Ionization Mass Spectrometry (CI-MS)

Proton-transfer-reaction (PTR) mass spectrometry is a powerful and widely used technique, yet it has drawbacks for some analyses. Chief among these is a high degree of fragmentation of certain functional groups, especially alcohols, peroxides, esters, and other highly oxidized molecules. NH_4^+-adduct ionization is much lower energy, or “softer,” than proton-transfer-reaction, producing mass spectra with less fragmentation, especially for key functional groups. Figure 5 shows Vocus CI mass spectra of the terpene aldehyde 2,6,10-trimethylundec-9-enal (farenal, MW 210 Da, fragrance compound), acquired with H_3O^+ and NH_4^+ reagent ions. When ionized by H_3O^+, farenal fragments by pathways common to PTR-MS, including dehydration of the aldehyde group. In contrast, the farenal-NH_4^+ adduct is the dominant peak in the NH_4^+ mode spectrum, with negligible fragmentation.

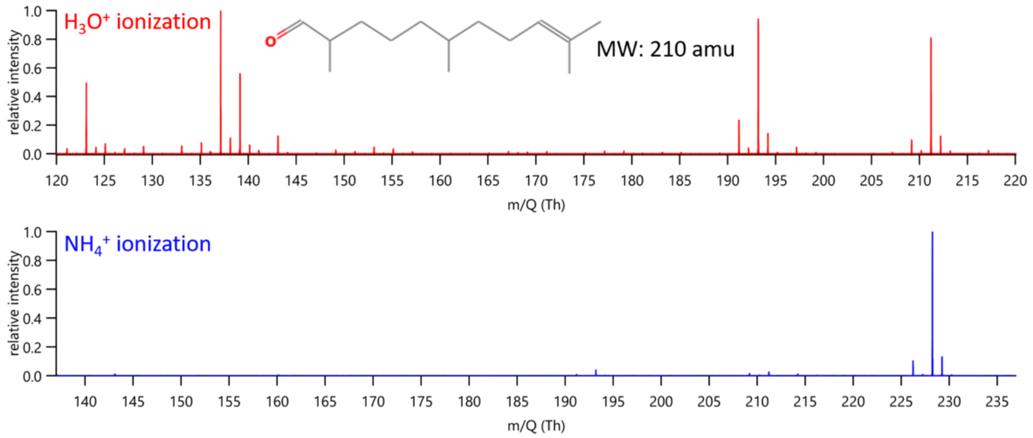

Figure 5 *Comparison of Vocus CI mass spectra of farenal measured with H_3O^+ (top) and NH_4^+ ionization (bottom). The structure of farenal is shown in the top panel.*

Additionally, while conventional PTR is a “broadband” technique that ionizes a wide variety of volatile organic compounds (VOCs), NH_4^+ is a selective technique, meaning that it is far more sensitive to certain groups of VOCs than others. This is especially helpful in situations where NH_4^+ chemical ionization has a high sensitivity for a target analyte that is found in low abundance in a complex matrix with high concentrations of non-target VOCs. For example, crude oil contains high concentrations of aromatics (BTX), which rapidly deplete the H_3O^+ reagent ions used for PTR chemical ionization. The binding energy of the NH_4^+-aromatic adduct is weaker, allowing other VOCs in petroleum to be measured while small aromatics are ignored.

Collision-Induced Dissociation: Direct, Fast Quantification of Complex Substances

A major challenge of online mass spectrometry is the quantification of measured compounds (the determination of sensitivity). Often, dozens to hundreds of compounds are measured, and calibration of each with a cylinder or other calibration system is far too time-intensive and expensive to do practically. Many species of interest are difficult or impossible to purchase commercially or synthesize in significant amounts; others react or decompose in conventional calibration systems. Collision-induced dissociation is a method that overcomes these challenges by determining the sensitivity to all species in a sample of interest directly, simultaneously, and in near real-time. Collision-induced dissociation methods are often used in MS-MS to identify compounds based on their fragmentation. In contrast, when used with NH_4^+ chemical ionization, low-energy CID is used to dissociate the NH_4^+ ion adduct from the VOC molecule, rather than fragmenting the VOC.

In adduct-based CI-MS, the sensitivity is related to the collision frequency and the transmission of the adduct to the detector. The collision frequency is determined by the instrument temperature and pressure settings, given fixed sampling flow. The transmission of the adduct depends partly on the binding energy of the reagent ion to the VOC analyte molecule: weakly bound clusters dissociate easily, are transmitted less efficiently to the detector, and are therefore detected less sensitively. The binding energy has a unique value for each VOC. Binding energies can be calculated, but these calculations are computationally expensive and must be done by an expert. It is easier to empirically measure the binding energies. This is done by scanning through a range of voltages applied to ion-optic electrodes near the exit of the Vocus IMR. When the voltage is higher, ion energies are higher, and adducts dissociate. The stability of a particular detected VOC-adduct ion can be parameterized by the fraction of adducts that dissociate at each voltage (Figure 6).

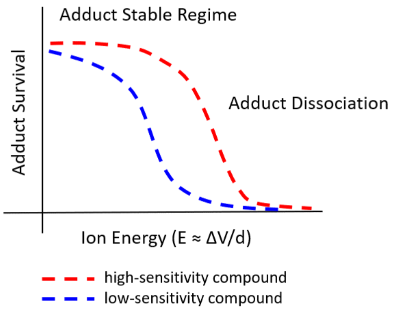

Figure 6 Basic principle of sensitivity determined by collision-induced dissociation. High-sensitivity compounds form stable adducts with large binding energy, which can survive high-ion-energy conditions in the instrument. Low-sensitivity compounds dissociate at lower energies. The sensitivity can therefore be parameterized by the voltage.

Once the binding energy of all detected VOC-adducts is determined, it can be converted to sensitivity by interpolating from the sensitivities and binding energies of a small number of compounds from a separate, single-time measurement of a standard cylinder.

Example Applications of NH_4^+-Adduct CI-MS

NH_4^+-adduct CI-MS is ideal for a wide range of applications. Here we show examples from several disparate fields that demonstrate the advantages of NH_4^+ CI-MS for soft, sensitive and selective measurement of a target group of species, and how synergies with PTR-MS expand the measurement capabilities of a Vocus chemical ionization mass spectrometer.

Security

Peroxide-based explosives are of particular interest to the law enforcement community. These highly oxidized compounds fragment easily when detected with conventional PTR-MS but are detected sensitively and selectively with NH_4^+-adduct CI-MS. Triacetone triperoxide (TATP) is one such compound. Trace TATP emitted from a canine-training aid carried by an individual can be detected in real time at parts-per-trillion level (Figure 7).

Explosives are difficult to quantify because of the difficulty of introducing them into conventional calibration systems. In Figure 8, trace amounts of hexamethylene triperoxide diamine (HMTD), a low-vapor-pressure explosive, are precisely quantified using the collision-induced-dissociation method.

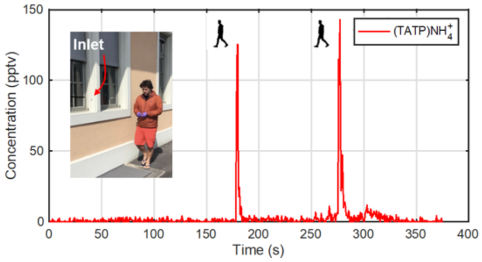

Figure 7 *An individual carrying a small sample of TATP walked twice past a window with the NH_4^+ CIMS instrument inlet. Trace levels of TATP were detected sensitively.*

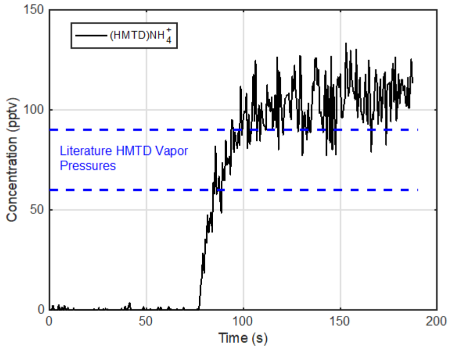

Figure 8 *A sample of HMTD was opened after approximately 70 seconds and measured using NH_4^+-adduct CI-MS. Use of collision-induced-dissociation to quantify the instrument sensitivity to this compound determined a 1-second limit-of-detection of less than 1 pptv.*

Breath

Using NH_4^+ reagent ions, the Vocus CI mass spectrometer can directly measure low-concentration metabolites and other compounds in breath with reduced fragmentation relative to PTR. Figure 9 shows Vocus CI-MS measurements of individual breaths with H_3O^+ (PTR) and NH_4^+ reagent ions. The test subject ingested a eucalyptol capsule (molecular formula $C_{10}H_{18}O$), and the exhaled metabolites were monitored in real time. The reduced fragmentation of the NH_4^+ spectra makes the technique better suited for untargeted analysis.

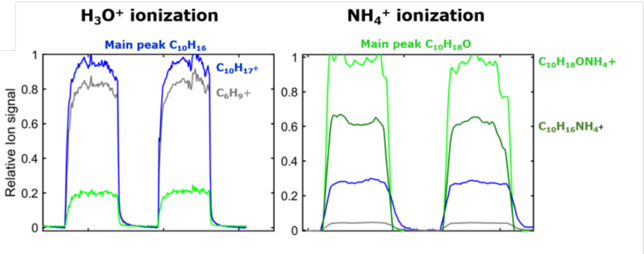

Figure 9 *Exhaled breath containing eucalyptol and metabolites. Left: two breaths measured with H_3O^+ reagent ions. Right: additional breaths measured with NH_4^+ reagent ions, showing reduced fragmentation of monoterpenes and more selective measurement of oxygenated compounds.*

Environment

PTR-MS is an essential tool in atmospheric chemistry. The use of NH_4^+-adduct CI-MS enhances field and laboratory measurements by capturing highly-oxidized molecules important for the formation of fine particulates. An example of measurements of products resulting from ozone-initiated oxidation of α-pinene in a flow tube is shown in Figure 10. The figure shows a binding-energy scan of oxidation products containing up to seven oxygen atoms.

Most oxygenated adducts are more strongly bound than simple ketones, because more oxygen and polar functional groups leads to stronger binding. In general, oxidized organic molecules generally form strong, stable adducts. The adduct formation reactions are fast, so compounds are ionized at near the collision limit.

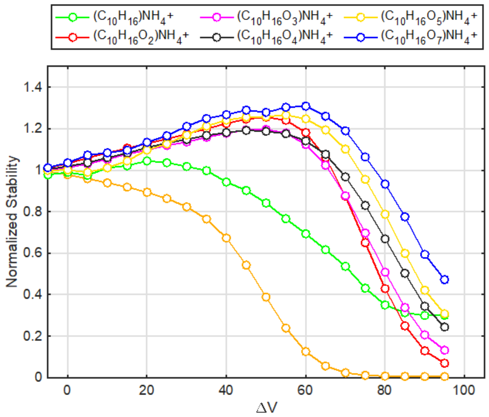

Figure 10 *Example CID scan of highly oxidized molecules resulting from α-pinene oxidation. Highly oxidized compounds dissociate at much higher energies than simple ketones (such as MEK, shown in orange for reference).*

Petrochemistry

Volatile organic compounds found in petroleum are dominated by alkanes, cyclolkanes, and aromatics. However, these compounds are not relevant to economically important analyses that determine the acidic and sulfur content. Use of NH_4^+ CI-MS to measure volatiles from crude oil highlights oxygen, sulfur, and nitrogen-containing functional groups, without being overwhelmed by the hydrocarbons present in the sample. In the NH_4^+ adduct CI-MS data shown in Figure 11, hundreds of individual species present in crude oil headspace are visible, with no sample preparation and measurement time of less than a minute.

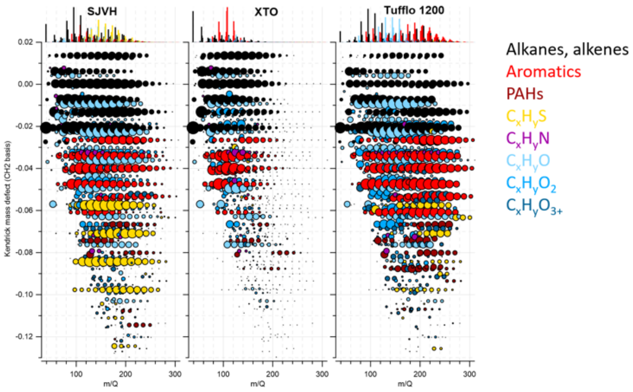

Figure 11 *Headspace sample of three different crude oils (SJVH, XTO, and Tufflo 1200). A mass spectrum of each is shown at the top. The Kendrick mass defect plot on the bottom separates compounds by functional group (y-axis) and molecular weight (x-axis). The size of the dot indicates compound abundance, and color indicates the elemental composition. Many sulfur-, nitrogen-, and oxygen-containing compounds are visible.*

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