Detection and Identification of Illicit and Hazardous Substances with Proton-Transfer-Reaction Mass Spectrometry (PTR-MS)

Abstract

The innovative Proton-Transfer-Reaction Mass Spectrometry (PTR-MS) technology was invented and developed in the 1990s by scientists at the "Institut für Ionenphysik" at the Leopold-Franzens Universität in Innsbruck and was commercialized by the spin-off company IONICON Analytik GmbH. PTR-MS rapidly became a well established analytical technology in the fields of environmental research, atmospheric chemistry, and food and flavor science [1]. This resulted from its high selectivity (up to 8 000 m/Δm), extremely low detection limits (sub-pptv levels), rapid response times (100 ms) and real-time quantification capability.

Here we present our latest studies on using PTR-MS in the analysis of explosives (TNT, RDX, PETN, Semtex, etc.) in the gas and in the liquid phase, as well as chemical warfare agents (CWAs) and illicit, prescribed and designer drugs [2-4]. It turns out that PTR-MS can detect all of these substances even in smallest concentrations with high selectivity. Therefore, even in a complex chemical environment we are able to detect threat agents with high levels of confidence, thus nearly eliminating so-called "false positives".

Moreover, from the beginning of 2008 until 2011, Ionicon was a partner in the European Defence Agency (EDA) JIP-FP project "GUARDED". In this three-year project, we developed a rugged and compact PTR-MS instrument for use on a robot platform. Details about the outcome of this project will be presented.

1 Experimental setup and technical developments

1.1 Experimental setup

In a typical PTR-MS instrument [2] water vapor originating from a reservoir filled with distilled water enters a hollow cathode ion source, where the H_2O is transformed into H_3O^+ (primary ions). Due to the sophisticated design of the ion source, this process is highly efficient, i.e. the purity of the primary ions is greater than 99%, which means that no signal-diminishing mass filter (as is used by techniques like e.g. SIFT-MS) is needed between the ion source and the adjacent drift tube. The actual ionization of the trace compounds present in the sample air takes place in the drift tube via proton transfer from H_3O^+ to all molecules that possess a higher proton affinity than water. As all major air components (N_2, O_2, CO_2, Ar, etc.) have lower proton affinities than water, the air itself acts as a buffer gas and no additional gas supply is needed for the operation of a PTR-MS instrument. Depending on the kind of instrument the protonated molecules are subsequently introduced into either a quadrupole mass filter or a time-of-flight (TOF) mass analyzer. Figure 1 presents a schematic drawing of a TOF based PTR-MS instrument.
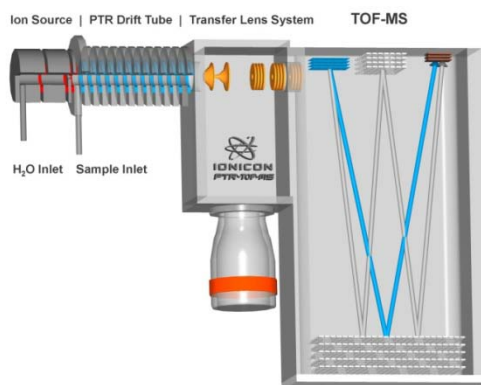
**Figure 1** Schematic drawing of a PTR-TOF-MS.

1.2 Latest technical developments

Some of the latest instrumental developments we want to report here are: (i) the improvement of the detection limit that now allows for measuring trace gas compounds in a concentration range from several ppmv down to the ppqv (parts-per-quadrillion) region with a typical response time well below 100 ms, (ii) the coupling of the sophisticated PTR source to two different types of time-of-flight (TOF) mass analyzers (one with an outstanding mass resolution called PTR-TOF 8000 [3] and one with an increased sensitivity called PTR-TOF 2000 [4]) and (iii) the possibility to switch between H_3O^+, NO^+ and O_2^+ as reagent ions [5].

Development (i) allows for entering new fields of application where extremely high sensitivities are needed. Explosives for example possess very low vapor pressures and are therefore difficult to detect in the gas phase. We performed proof-of-principle measurements where we could detect and identify all of the common solid explosives (RDX, TNT, PETN, etc.) by analyzing the headspace above small quantities of samples at room temperature and also from trace quantities not visible to the naked eye placed on surfaces [4].

The use of TOF detectors in (ii) is especially important for applications where not only high sensitivity but also unambiguous identification is needed (e.g. detection of chemical warfare agents

[6] while avoiding false positive alarms). The high mass resolution of up to 8.000 m/Δm and accuracy of the PTR-TOF 8000 allow for separation of most isobaric compounds (see Figure 2 for an example) and for substance identification via the exact mass. As there might be applications where an enormous mass resolution is not necessarily needed but the sensitivity has to be as high as possible, the PTR-TOF 2000 performs with an enhanced sensitivity at the expense of a somewhat lower mass resolution. Comparison data demonstrate that the resolution of this PTR-TOF 2000 is still around 2.000 m/Δm while showing an increased sensitivity by a factor of five compared to the PTR-TOF 8000.
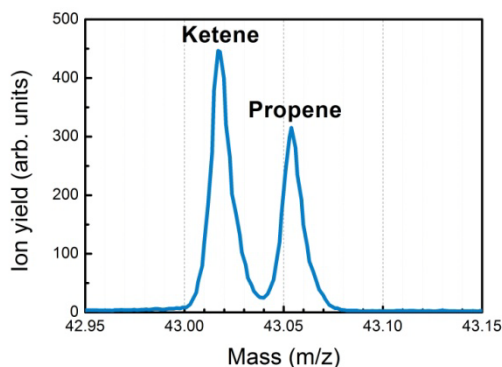
**Figure 2** Separation of the two isobars ketene (43.018 m/z) and propene (43.055 m/z) with a PTR-TOF 8000

For iii) we see that the sensitivities obtained with NO^+ and O_2^+ are comparable or even better than the outstanding sensitivity of the established PTR-MS instruments and therefore well above those from e.g. SIFT-, IMR- and other CI-MS instruments for trace gas analysis. To demonstrate the advantages of this so called "SRI" (switchable reagent ions) setup we measured e.g. acetone and propanal (isomeric molecules at nominal mass 58 amu) utilizing NO^+ as the precursor ion. According to Spanel et al. [7] NO^+ interactions with aldehydes follow the reaction: $NO^+ + XH \rightarrow X^+ + NOH$ whereas ketones follow: $NO^+ + XH \rightarrow XH^+ + NO$ (and clustering). This means that we see isomeric compounds on different nominal masses and can identify them unambiguously. Furthermore, by using O_2^+ precursor ions we are able to ionize molecules via charge transfer reactions that cannot be measured via hydronium proton transfer reaction (e.g. ethylene). This means that they are now detectable with PTR+SRI-MS instruments.

Although PTR-MS is an outstanding technology for trace gas analysis it has one drawback: trace compounds dissolved in liquids can only be measured via headspace analysis or membrane inlet setups. Both sampling methods are suitable for certain applications, but suffer also from a number of disadvantages. The direct aqueous injection (DAI) technique developed by us turns out to be an ideal solution for direct analysis of liquid samples with PTR-MS. After successful proof-of-principle measurements in [8] we presented first data possibly leading to real-life applications, namely the contamination of water (e.g. lakes) with explosives from dumped bombs / ammunition sites [9].

In DAI a carrier airstream generated by a diaphragm pump is cleaned and dried in an activated charcoal filter and a cooling trap. Thereafter the exact amount of clean and dry air of this carrier gas line entering the injection region is adjusted by a mass flow controller and subsequently heated in a thermostatic heating box to ensure that all parts are at the same temperature, so that no condensation on cold spots can occur. The needle of a syringe holding the sample liquid is pierced through a septum which seals one of the openings of a T-piece mounted in the carrier gas line. The injection speed is controlled by a high precision syringe pump.

2 Experimental data

2.1 Solid explosives

In [4] we described proof-of-principle measurements showing that PTR-MS is able to detect all common explosives like 1,3,5-triazine hexahydro-1,3,5-trinitro (RDX), 2,4,6-trinitrotoluene (TNT), pentaerythritol tetranitrate (PETN), etc. While the measurements of the headspace of small quantities (a few mg) of the above-mentioned substances proved that the sensitivity of a PTR-TOF 8000 is sufficient for detecting them without the need of pre-concentration or heating, the scientifically most interesting results came from so-called E/N investigations, i.e. measuring the ion yield as a function of the reduced electric field strength. As the E/N value, which can mainly be controlled by changing the applied voltage on the PTR drift tube, is proportional to the collision energy between the reagent ions and the sample molecules, usually fragmentation can be suppressed by choosing lower drift tube voltages or enforced by choosing higher voltages respectively. This behavior is not only true for many molecules investigated so far with PTR-MS but also for the explosives PETN and RDX, where the highest protonated parent ion yield, i.e. lowest level of fragmentation could be obtained by lowering the drift tube voltage and therefore the E/N value (from usually 600V to about 350V). Figure 3 shows the E/N investigation for TNT. Although preliminary measurements by us on the explosive 1,3,5 trinitrobenzene (TNB) indicate a similar E/N behavior of TNB, we could not find any reports in literature of other molecules showing such a behavior. One possible explanation for the huge difference of about one order of magnitude between 90 and 180 Td in the ion yield of the protonated TNT parent ion could be clustering, e.g. with water molecules, which is suppressed at higher E/N values. However, by recording mass spectra up to about 1000 m/z we could rule out this possibility, so that the E/N behavior of TNT still remains unexplained.
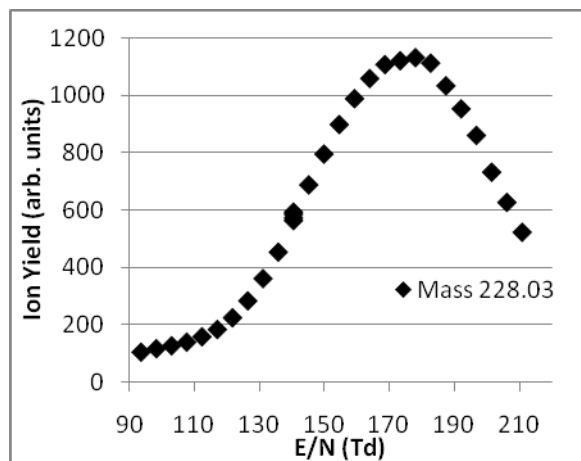
Figure 3 Ion yield of the protonated parent ion recorded from the headspace of TNT as a function of the reduced electric field (E/N).

Regardless of the fact that at present we are unable to provide an explanation for TNT (and TNB) showing a higher ion yield at elevated E/N values, this observation has a great potential in the unambiguous identification of TNT. In addition to the rather high level of confidence in substance identification using the exact mass, which would in case of a PTR-TOF 8000 already be sufficient for separating e.g. protonated nitroglycerin (NG; 228.010 m/z) from protonated TNT (228.025 m/z), comparing the ion yields at a rather low and a rather high E/N value could make the identification

even more certain, as the TNT signal should drop about one order of magnitude at low E/N and the NG signal should increase.
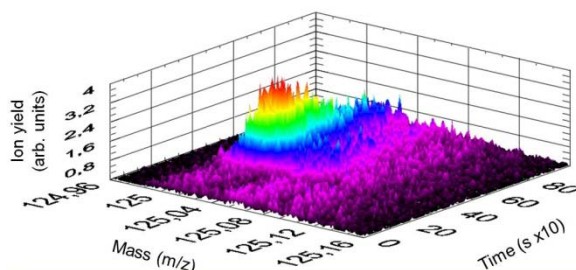
2.2   Chemical warfare agents

Also for CWAs we started off with proof-of-princple measurements [6]. In contrast to the explosives which were provided by the University of Innsbruck we did not have access to real CWAs, so we had to use simulants for the present studies, namely dimethyl methylphosphonate, diethyl methylphosphonate, diisopropyl methylphosphonate, dipropylene glycol monomethylether and the mustard gas analog 2-chloroethyl ethyl sulfide (2-CEES). As all these CWA (simulants) possess by definition rather high vapor pressures we could detect them easily in the headspace. The signal was so high that we had to wash the vials containing a droplet of the substance repeatedly with distilled water and do the investigations on the remaining traces in the vials to avoid saturation of the detector. Also the substance identification could be performed at very high levels of accuracy based on the exact mass, characteristic fragments and isotope ratios.

Besides these fundamental tests of detectability we performed a "real-life" test (see Figure 4) by placing the PTR-TOF 8000 inlet in the middle of our 60 m³ laboratory. Subsequently we turned off the HVAC system and opened a vial containing the mustard gas analog (2-CEES; at around 300 s in Figure 4). Already seconds after opening of the vial the PTR-MS instrument displays an increase on the exact mass of protonated 2-CEES which continues until the vial is closed again. After turning on the HVAC system the 2-CEES concentration slowly decreases with time.

Figure 4 3D view of the ion yield originating from a mustard gas analog spreading in lab air.

This very preliminary test could act as a basis for the FP7-SEC project "SPIRIT" in which Ionicon is partner. In this project a PTR-MS instrument should be adapted in a way so that it monitors the HVAC system of an endangered building at sets of an alarm as soon as a harmful substance is detected.

2.3 Illict and designer drugs

Table 1 lists all illicit [10] and designer drugs investigated by us so far. Again, small amounts (about 50 mg) of each drug were placed in vials and the headspace was investigated and could be detected and identified easily.

Category	Drug	m/z
Illicit drugs	Heroin	370.17
	Cocaine	304.15
	Codeine	300.16
	Morphine	286.14
	Ecstasy (MDMA)	194.12
Designer drugs	Dimethocaine	279.20
	2C-D	196.13
	Ethcathinone	178.12
	4-Fluoroamphetamine	154.10
"Rape" drugs	1,4-Butanediol	91.07
	gamma-Butyrolactone	87.04

Table 1 Overview of all illicit and designer drugs investigated by us so far.

Especially for designer drugs, where new substances appear on the market frequently, one advantage of PTR-MS becomes obvious. As many established detection methods (e.g. test strips) only detect substances for which they are made for, PTR-MS can virtually detect every drug, even the very new ones.

As there are drugs which are predominantly consumed highly diluted in liquids, we extended our headspace studies to gamma-butyrolactone (GBL) and 1,4-butanediol (BDO) traces mixed in different concentrations into plain water, tea, red and white wine. Both substances are metabolized in the human body to gamma-hydroxybutyric acid ("liquid ecstasy") and are therefore frequently abused as recreational drugs (in lower doses) or so-called "rape drugs" (in higher doses). With the DAI system coupled to PTR-MS we were able to detect both substances in all above-mentioned liquids with great linearity down to concentration levels far below the activation threshold for effects in human beings.

Figure 5 shows one exemplary measurement of GBL mixed in red wine at different concentrations. Comparable results were obtained in white wine, tea and tab water.
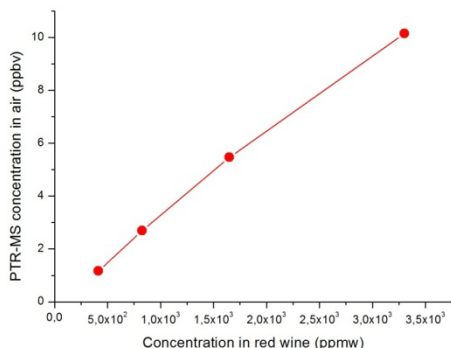
Figure 5 GBL mixed in red wine at different concentrations and detected with the DAI system coupled to PTR-MS.

3   JIP-FP project "GUARDED"

The official abstract of the Joint Investment Programme - Force Protection (JIP-FP) "Generic Urban Area Robotized Detection of CBRNE Devices" (GUARDED) in which Ionicon was a partner reads according to the official website of the European Defence Agency (EDA):

"*The aim of this project is to demonstrate a remote controlled mobile platform for sniffing a suspect and/or dangerous area, having on board a set of complementary CBRNE sensors to provide a safe diagnostic obtained through data fusion between various sensors, enabling weddings and solving the old paradox of the need for compromising between resolution and detection. Therefore, after a state of the art of various detection techniques allowing to give an overview of what can be detected and how nowadays, use cases scenarios will be established with the help of operational experts to place the project in a realistic context. From then, an intensive trials campaign will conducted. Technologies like Ground Penetrating Radar techniques for localisation, even through walls or buried objects, Proton transfer Reaction coupled with Mass Spectrometry, Chemical and Biological based on handheld devices and improving new sampling techniques etc. will be used. To validate the approach, a trial period is planned after the integration & tests phase, which is traditionally crucial, allowing to point out and measure the effects of the project, i.e. completion of the inspection & securing mission.*"

Already in the first phase of planning it became clear that GPR and IMS are technologies for a quick and approximate estimation whether an illicit substance is present or not. In contrast, PTR-MS can identify and quantify substances at a very high level of accuracy while on the other hand consuming more space and payload on the robot platform. Therefore it was decided that two platforms would be built, one carrying the "exploratory" sensors and one the more exact PTR-MS. From the beginning of 2008 until 2011 Ionicon developed a rugged and compact PTR-MS instrument for being used on a robot platform. Starting from the established "Compact PTR-MS" model we performed some preliminary tests in a real-life scenario, i.e. sniffing paper boxes containing explosives, chemical warfare agents, toxic industrial compounds and harmless everyday substances. Based on these results we went on with detailed analysis of the different substances in their pure form in the lab. Furthermore we developed a simple form of a pre-concentrator coupled with thermal desorption and integrated it into the final GUARDED prototype. The software interface had to be fundamentally adapted. Starting from the established "PTR-MS Control" software that gives as much information as possible about the measurement process

(instrumental parameters, voltages, masses, count-rates, temperatures, etc.) we developed a highly user-friendly and flexible graphical user interface (GUI) for the fully automated instrument. Now the operator does not need specific knowledge about chemistry or physics but sees directly on the display which of the pre-set substances have been detected and at which threat level. The whole system is entirely computer controlled via an embedded PC that is continuously monitoring the system status and providing a high level of safety, e.g. by turning off the voltage supplies in case of a vacuum failure, etc. A second embedded PC with Windows CE as an operating system acts as the platform for the installed GUARDED GUI. Additionally this prototype is equipped with a simple form of a pre-concentrator combined with thermal desorption. A high-power fan draws large amounts of (contaminated) air for a pre-defined time through a fine metal mesh. As especially vapors from explosives are known to be very adhesive, the common harmless air compounds will pass through the mesh whereas the explosive vapors will stick to it. After several seconds the fan is turned off and a current running through the mesh is ohmically heated. The evaporating explosive molecules in their concentrated form are then directly drawn into the PTR drift tube via a heated capillary.

The laptop computer controlling the instrument and displaying the results is connected via common WiFi. In addition the instrument itself is equipped with a touch-screen display that can be used for displaying the measurement results, i.e. alarms, substance identification, etc. Thus, the PTR-MS can be used as a "standalone" instrument, i.e. without the need of an external computer.

The GUARDED prototype is installed in a box with roughly 55 cm side length and the previously mentioned pre-concentrator add-on is mounted on top. The whole system weights around 60 kg. With the aid of exactly dimensioned shock-absorbers the instrument is mounted on the robot platform provided by the project leader ECA (France), together with the battery pack that is needed for cordless operation of the PTR-MS.

Figure 6 shows the GUARDED platform "in action", i.e. a box containing traces of the infamous CWA chloropicrin is placed in a car trunk. The remote controlled platform approaches the trunk and as soon as the inlet comes close to the contaminated box the threat is identified and an alarm is set off.
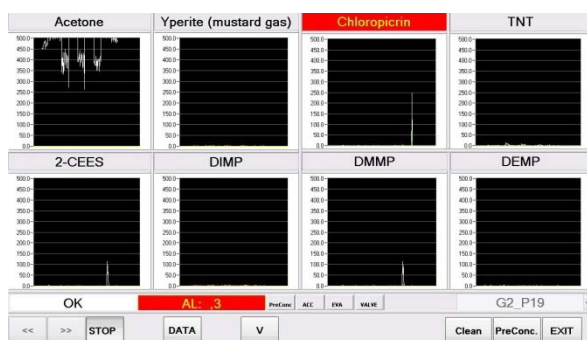
Figure 6 GUARDED robot platform approaching a suspicious box in a car trunk (top) and an alarm for chloropicrin is set off on the laptop computer connected to the platform via WiFi (bottom).

4   Conclusions

With the present results we showed that PTR-MS is capable of detecting and identifying virtually every substance that can be a threat to society. In the framework of the GUARDED project we demonstrated that this is true not only for the previously published proof-of-principle investigations in a lab environment but more importantly also under real-life conditions, i.e. in public places like a car park. In the near future we are planning to adapt also the inlet system which is at the moment (besides from the pre-concentrator prototype) not optimized for the sampling of very sticky compounds like e.g. explosives or CWAs. Possible solutions could be utilizing alternative materials or devices like e.g. thermal desorption strips like they are used in combination with IMS instruments at airports or at customs.

Acknowledgement

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