ANALYSIS OF TRACE GASES AT ppb LEVELS BY PROTON TRANSFER REACTION MASS SPECTROMETRY (PTR-MS).

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Abstract

A proton transfer reaction mass spectrometry (PTR-MS) system has been developed which allows for on-line measurements of trace gas components with concentrations as low as 1 ppb. The method is based on reactions of H$_3$O$^+$ ions, which perform non-dissociative proton transfer to most of the common organic trace constituents but do not react with any of the components present in clean air. Examples of medical information obtained by means of breath analysis, of environmental trace gas analysis, and examples in the field of food chemistry demonstrate the wide applicability of the method.

1. Introduction

Gas chromatographic methods have been refined over the past decades, so that they allow for the quantification of trace gas components in the ppt regime. They are however not well suited for on-line investigations of strongly time dependent concentrations. Mass spectrometry on the other hand is extremely fast but on-line gas analysis based on conventional mass spectrometry using electron impact ionization suffers from the strong fragmentation of molecular ionic species [1]. Especially when a mixture of organic components is to be analyzed, the complexity of breakup patterns puts severe constraints on the quantitative analysis of the concentrations of these components. Recent attempts to use thermal charge transfer processes to ionize the neutrals to be analyzed showed some improvement in that the breakup of the molecular components could be significantly reduced [2].

Even better results were obtained by using proton transfer reactions, for the ionization of trace constituents [3]. When H$_3$O$^+$ is used as the proton donor, most of the typical organic trace components M$_i$H$_j$ (where M is a combination of C, O, N and S atoms) in air are ionized by proton transfer processes,
These reactions are invariably fast, whenever they are exoergic, with rate coefficients, \( k \), close to the collisional limiting values, \( k_o \approx 10^{-9} \text{cm}^3\text{s}^{-1} \) (\( k_o \) is the Langevin rate coefficient, \( k_L \), in the case of non-polar neutrals [4] or the capture rate coefficient, \( k_c \), in the case of polar neutral reactants [5]). \( \text{H}_2\text{O} \) has a proton affinity of 7.22 eV [6], and common organic molecules have proton affinities in the range from 7 to 9 eV (Table I), thus making most of the relevant proton transfer reactions involving \( \text{H}_3\text{O}^+ \) ions slightly exoergic, but keeping the exoergicity low enough, so that breakup of the neutrals to be detected only seldom occurs.

<table>
<thead>
<tr>
<th>Component</th>
<th>Proton Affinities</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>[kcal/mol]</td>
</tr>
<tr>
<td>He</td>
<td>42.5</td>
</tr>
<tr>
<td>Ne</td>
<td>48.1</td>
</tr>
<tr>
<td>Ar</td>
<td>88.6</td>
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<tr>
<td>( \text{O}_2 )</td>
<td>100.9</td>
</tr>
<tr>
<td>( \text{N}_2 )</td>
<td>118.2</td>
</tr>
<tr>
<td>( \text{CO}_2 )</td>
<td>130.9</td>
</tr>
<tr>
<td>( \text{CH}_4 )</td>
<td>132</td>
</tr>
<tr>
<td>( \text{N}_2\text{O} )</td>
<td>136.5</td>
</tr>
<tr>
<td>CO</td>
<td>141.9</td>
</tr>
<tr>
<td>( \text{H}_2\text{O} )</td>
<td>166.5</td>
</tr>
<tr>
<td>( \text{C}<em>4\text{H}</em>{10} )</td>
<td>163.3</td>
</tr>
<tr>
<td>( \text{H}_2\text{S} )</td>
<td>170.2</td>
</tr>
<tr>
<td>HCN</td>
<td>171.4</td>
</tr>
<tr>
<td>( \text{C}_6\text{H}_6 )</td>
<td>181.9</td>
</tr>
<tr>
<td>( \text{C}_3\text{H}_6 )</td>
<td>179.8</td>
</tr>
<tr>
<td>HCOOH</td>
<td>178.8</td>
</tr>
<tr>
<td>( \text{CH}_3\text{OH} )</td>
<td>181.9</td>
</tr>
<tr>
<td>( \text{CH}_3\text{CN} )</td>
<td>188.0</td>
</tr>
<tr>
<td>( \text{CH}_2\text{COH} )</td>
<td>186.6</td>
</tr>
<tr>
<td>( \text{C}_2\text{H}_5\text{OH} )</td>
<td>188.3</td>
</tr>
<tr>
<td>( \text{CH}_3\text{COCH}_3 )</td>
<td>196.7</td>
</tr>
<tr>
<td>NH(_3)</td>
<td>204.0</td>
</tr>
</tbody>
</table>

Table I Proton affinities of common components in clean air and of various organic compounds [from Ref. 6]
PTR-MS [3] was demonstrated to be applicable for trace gas analysis by using a conventional Selected Ion Flow Drift Tube (SIFDT) [7]. H$_3$O$^+$ ions originating from a high pressure electron impact ion source were preselected by means of a quadrupole mass filter and injected into the drift zone of the Innsbruck SIFDT, which was operated with helium buffer gas. PTR-MS using the Innsbruck SIFDT-apparatus has been successfully applied so far to perform on-line measurements of trace components in the human breath, such as ethanol, methanol and acetone [3,8]. The limits for the quantitative analysis of these components were mole fractions of about 0.1 ppm.

Recently a new PTR-MS-system was developed, the sensitivity of which was increased by two orders of magnitude, so that trace constituents in air in the order of 1 ppb are measurable in on-line experiments. This allows for the investigation of concentrations of components such as benzene, acetonitrile, isoprene, and dimethyl sulfide and others in the human breath, acetaldehyde, formaldehyde, methanol, ethanol and others in buildings as well as in ambient air. A brief description of the new system is presented in the following.

**Experimental**

The apparatus (a schematic drawing of which is shown in Fig. 1) consists of a conventional drift tube equipped with a hollow cathode ion source which produces H$_3$O$^+$ ions with only traces of impurity ions (mainly O$_2^+$), so that no mass spectrometer is needed to preselect H$_3$O$^+$ before injection into the drift tube.

![Schematic representation of the PTR-MS apparatus](image)

Fig. 1 Schematic representation of the PTR-MS apparatus. HC hollow cathode; SD drift region; VI Venturi type inlet.
In this way a high primary ion signal is detected at the downstream end of the drift tube, which is a necessary prerequisite to achieve a high sensitivity of the system. The air to be analyzed acts itself as the buffer gas (the pressure is \( \sim 10^{-1} \) Torr) in the drift tube. This is possible because \( \text{H}_3\text{O}^+ \) does not react with any of the natural components of air, as they all have lower proton affinities than \( \text{H}_2\text{O} \). On the other hand \( \text{H}_3\text{O}^+ \) performs proton transfer in nondissociative reactions,

\[
\text{H}_3\text{O}^+ + \text{R} \xrightleftharpoons[k]{} \text{RH}^+ + \text{H}_2\text{O} \tag{2}
\]

with many volatile organic compounds, \( \text{R} \), with large rate constants, \( k \), equal to the collisional limiting values (\( \approx 10^{-9}\text{cm}^3\text{s}^{-1} \)) [9].

The density \( [\text{R}] \) of a neutral impurity \( \text{R} \) is calculated from the count rates \( i(\text{RH}^+) \) and \( i(\text{H}_3\text{O}^+) \) obtained in the downstream ion detection system using the relation

\[
i(\text{RH}^+) = i(\text{H}_3\text{O}^+)_0 (1-e^{-k[R]t}) \approx i(\text{H}_3\text{O}^+)_0 [\text{R}] kt, \tag{3}
\]

where \( t \) is the time, the \( \text{H}_3\text{O}^+ \) ions need to pass the drift tube. \( t \) is calculated from known mobility values of \( \text{H}_3\text{O}^+ \) in air in the usual way [9].

An electric field \( E \) is applied along the drift tube in order to avoid substantial formation of cluster ions \( \text{H}_3\text{O}^+ (\text{H}_2\text{O})_n, n = 1,2, ..., \) which otherwise would be created in association reactions of \( \text{H}_3\text{O}^+ \) with water molecules present in the air to be analyzed. Increasing \( E \) and thus \( E/N \) (\( N \) being the number density of the buffer gas) leads to an increase of the relative kinetic energy, \( KE_{cm} \), between the reactants, which is calculated, when necessary according to standard procedures as described by McFarland et al. [9]. Usually, throughout the measurements, \( E/N \) is kept at values of 120 to 140 Td (1 Td = 1 Townsend = 10^{-17} \text{Vcm}^2) which makes \( KE_{cm} \sim 0.3 \text{eV} \), depending somewhat on the mass of the neutral reactant \( \text{R} \).

A more detailed description of the PTR-MS system has been published by Hansel et al. [10].

3. Applications

In the following we will present a variety of examples showing the wide applicability of PTR-MS in the field of medicine, environmental research and food chemistry.

a) Medical Applications.

The exhaled human breath contains the natural constituents of air but also a variety of endogenous volatile organic compounds (VOC). The most abundant
ones of these are acetone, methanol, ethanol, propanol and isoprene. Acetone is normally present in concentrations of ~ 1 ppm while the others have concentrations of typically one to a few hundred ppb. Besides these abundant compounds there are amounts of just a few ppb of about 20 other compounds, such as benzene, acetonitrile, diallyl sulfide, allyl methyl sulfide, diallyl disulfide just to mention a few of them. These compounds are produced within the human body in metabolic processes. If these processes are influenced externally by intake of unusual amounts of specific foods or chemicals, many of the above compounds can show concentrations deviating significantly from the "normal" values. Oral ingestion of about half a gram of isopropanol (diluted in water) causes an increase of the acetone concentration in the breath by nearly two orders of magnitude within the next 20 minutes (Fig.2).

![Graph](image)

**Fig. 2** Concentration of acetone in the breath of a person after consumption of 0.45 g isopropanol.

Due to enzymatic action isopropanol is converted into acetone within the stomach and then resorbed to reach the blood stream. If the same experiment is done by taking the isopropanol intravenously, the concentration of isopropanol in the breath increases rapidly, reaching a maximum within one minute and declining thereafter again while acetone increases within about 1-3 minutes by a factor of about 50, staying at this enhanced level for the next hour. In this case the respective enzyme situated in the liver converts isopropanol to acetone,
which then takes a long time to be removed from the body. It is obvious that such kind of processes can be used for testing of the function of various organs in the body so that noninvasive diagnostic methods on the basis of PTR-MS will be developed in the near future.

Garlic has been used as an important dietary constituent and as a medicine for treatment of many disorders [11] in ancient times by the Egyptians, Greeks, Romans and ever since.

While intact garlic (Allium sativum) cloves hardly show any significant smell, crushed or cut garlic develops an extremely strong odour which also appears in the breath of persons who have consumed garlic [11,12]. The strong odour persists for time spans up to more than a day. The phenomenon is now well understood. Within the garlic cloves odorless alliin is stored in the mesophyll cells, well separated from an enzyme called alliinase, which is situated in the vascular bundle sheath cells [13]. When force acts on garlic cloves, so that cells are damaged by crushing or cutting, the enzyme comes in contact with alliin converting it to allicin which has a typical but not unpleasant odor like garlic [14]. Allicin in turn is converted into rather strongly smelling organosulfides, the chemistry of which has been investigated and described in great detail by Block [12].

Block et al.[11] also described early scientific investigations stimulated by the reputation of garlic as a "cure all", such as the work by Pasteur into garlic's antibacterial activity and work in 1892 by Wertheim and Semmler into the composition of distilled garlic oils (mainly diallyl disulfide). Also described are modern chromatographic investigations revealing degradation processes for allicin and other garlic thiosulfimates, particularly ally methyl thiosulfimates, in the presence of heat or organic solvents. These analytical investigations led to a better understanding of the reasons why garlic oil products show positive medical effects. For example diallyl disulfide is known to inhibit the activation of nitrosamine thus reducing the probability of the development of cancer of the stomach [12]. Ajoene, which forms by self-condensation from allicin in non-aqueous solvents is an efficient antithrombotic agent and allicin itself is antifungal as well as antibacterial.

In the breath of a test person the concentration of allyl methyl disulfide, diallyl sulfide, diallyl disulfid, and diallyl trisulfide rises to a maximum concentration shortly after ingestion of garlic and declines to normal baseline values within the next two to three hours. These four components are also present in the head space air sampled from crushed garlic.

In contrast to these compounds, allyl methyl sulfide, dimethyl sulfide and acetone increase much more slowly after garlic ingestion (Fig. 3.). -allyl methyl sulfide reaches a maximum of about 900 ppb after 4-5 hours then declining quite
Fig. 3 Concentration of allyl methyl sulfide, dimethyl sulfide, and acetone in the breath after consumption of garlic.

slowly such that more than a day later substantial concentrations of 100-250 ppb are still detected. While allicin, the main component in the extract from crushed garlic [12] is observed also in the head space air of garlic, it is not present in the exhaled air of the test person. Probably allicin is metabolized very quickly in the human body as may be expected from the observation by Lasskso et al. [14], that allicin is quite unstable in a fatty oil extract.

Quite remarkable is the observed increase of the acetone concentration in the breath of the test person which rose from 1.8 ppm to 5 ppm after 24 hours. Enhanced levels of acetone are observed in persons suffering from diabetes. Healthy persons show higher concentrations of acetone after fasting for more
than 10 to 15 hours or after performing strong exercise for typically more than 2 to 3 hours. In these cases the human body has fully exploited its sugar reserves in the blood and thus has started metabolizing its fat reserves which results in the production of acetone. In this context observations of Baksh and Chughtai [15] are worth noting that levels of serum cholesterol, serum triglycerides, serum total lipids and serum glucose increased significantly, when human subjects were given a fat rich diet for seven days. No such increase was observed, when substantial amounts of garlic were added to the same fat rich diet. The present observation of a moderate enhancement of acetone production after ingestion of garlic may be indicative of enhanced metabolism of fatty components in the bloodstream, thus reducing the above mentioned compounds. While acetone also was observed in the head space gas of crushed garlic, its concentration being about 10 ppm indicated too small amounts of acetone being contained in the garlic consumed by the test person in order to allow for the observed increase of acetone in the breath of the test person.

Isoprene concentrations in the breath increase significantly during sleep (Fig. 4) or tiredness, but its metabolism in the human body still is unknown. The average concentration in children is significantly lower (Fig. 5) than in adults, but also this observation is not at all understood up to now.

![Graph showing isoprene concentration in breath](image)

**Fig. 4** Concentration of isoprene in the breath of 7 persons.
b) Environmental

Using PTR-MS a wide variety of concentrations of various aromatic compounds have been measured in the air at a traffic crossing in Innsbruck. Assuming that these compounds are emitted directly from the exhausts of cars and lorries, i.e., that none of them is created by photochemical reactions, the densities of these compounds are proportional to the density of the traffic.
Fig. 6 shows a broad maximum in the morning from 7:30 to 9:00, a sharp maximum at lunch time and a pronounced peak at about 17:30. Additional compounds have also been investigated but are not shown in the figure.

Indoor air showed significantly higher concentrations of methanol, propanol, acetone and toluene in newly furnished homes as compared to old furnished rooms.

Oxygenated species in the atmosphere are important sources of free radicals and are intricately linked with the fate of nitrogen oxides (NOX) which are themselves necessary for tropospheric ozone formation. Crutzen and colleagues [16] have recently performed airborne measurements indicating the presence of significant concentrations of acetone and methanol in the free troposphere. On the basis of model calculations Crutzen and coworkers [17] conclude that the balance of the measured abundances and removal rates would require a global source of about 50 Tg yr\(^{-1}\) acetone and 45 Tg yr\(^{-1}\) methanol. It is assumed that most of the sources of tropospheric acetone and methanol are of natural origin, such as atmospheric oxidation of precursor hydrocarbons, like propane and isobutane as well as biogenic emissions from plants. Recently we have investigated the emissions of volatile organic compounds from dead biomaterial, such as leaves and needles and found quite remarkable emission rates in the range of 0.03 to 0.3 \(\mu g/g(DW)\) h\(^{-1}\) for acetone and for methanol (Fig. 7).

![Emission rates of methanol, acetone and isoprene from dead leaves as a function of the water content.](image-url)
On the assumption of a yearly growth of about $10^{16}$ g of biomaterial and the above emission rates occurring over an average time span of a year (needed for degradation of biomaterial) the emission of acetone and methanol by degrading biomaterial would be in the order of 2.5 to 25 Tg yr$^{-1}$ which would significantly contribute to the global sources of these compounds released into the free troposphere.

c) Food chemistry

When instant coffee is brewed, several brands of coffee develop a strong first burst of flavors after the water is added to the coffee powder. This burst of initial compounds was firstly measured on line in great detail by PTR-MS and Fig. 8 shows typical results on the time dependence of several aromatic compounds during the first few minutes. Similar investigations are in progress on tea and chocolate products as well as on the time dependent development of aromatic compounds during cooking of food.

![Graph showing time dependence of several VOCs in the first burst of instant coffee.](image)

Fig. 8 Time dependence of several VOC's in the first burst of instant coffee.

Especially in hot climate regions or generally in the summer there is always the danger that any kind of meat, which is not stored properly at low enough temperature may deteriorate to a degree where it no longer should be consumed [18]. PTR-MS provides a simple and fast working tool for controlling of the state of meat. Fig. 9 shows the emission of various compounds from a sample of meat purchased from a local supermarket and then being kept at room
temperature for about 50 hours. The data show a significant increase from a few ppb to more than 2000 ppb of the head space concentration of methane thiole and dimethyl sulfide starting rather sharply after 20 hours. The concentration of ethyl acetate increases continuously from 20 to 2000 ppb during the first 10 hours and stays at this level for the next 40 hours. Thus the head space composition of these compounds and others that have been investigated is a clear indicator of the degree of freshness or degradation of meat.

Fig. 9 Time evolution of several VOC's during degradation of meat stored at room temperature.

**Conclusion**

The wide applicability of PTR-MS for fast on-line measurements of trace constituents has been demonstrated by examples in the field of medicine, environmental research and food chemistry. Potential for further exploitation of the method will be noninvasive diagnostics of the function of organs in the human body, investigations of human metabolic processes, emissions from materials used for construction and furniture, monitoring of VOC emission from industrial plants, and especially on-line process monitoring of industrial fermentation and food production processes.
References


