Proton-transfer-reaction mass spectrometry (PTR–MS): on-line monitoring of volatile organic compounds at pptv levels

W. Lindinger, A. Hansel and A. Jordan

Institut für Ionenphysik der Leopold-Franzens-Universität, Technikerstr. 25, A 6020 Innsbruck, Austria

A system for on-line measurements of trace components with concentrations as low as a few pptv has been developed on the basis of proton transfer reactions. Medical applications by means of breath analysis allow the monitoring of metabolic processes in the human body, and examples of food research include investigations of volatile organic compound (VOC) emissions from fruit, coffee and meat. Investigations of VOC emissions from decaying biomatter and on-line monitoring of the diurnal variations of VOCs in ambient air are typical examples of environmental applications.

1 Introduction

On-line monitoring of trace compounds is becoming increasingly important, not only for industrial applications but also especially for measuring environmentally important constitutents. Therefore a wide variety of chemical ionization (CI) techniques have been developed over the past decades,[1] but many of these are laboratory bound and/or can be applied only to a limited number of compounds to be monitored simultaneously.

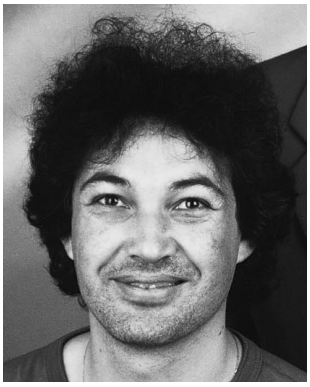
A proton-transfer-reaction mass spectrometer (PTR–MS) system which has been developed in our laboratory allows on-line monitoring of mixtures of volatile organic compounds (VOCs) at low concentrations. PTR–MS connects the idea of chemical ionization (CI), introduced by Munson and Field in 1966,[2] with the swarm technique of the flow-drift tube type (FDT) invented by Ferguson and his colleagues[3] in the early 1970s. We apply a CI system which is based on proton-transfer reactions, and preferentially we use H_3O^+ as the primary reactant ion which is the most suitable ion when air samples containing a wide variety of traces of volatile organic compounds (VOCs) are to be analysed.[4] Firstly, H_3O^+ does not react with any of the natural components of air, as they all have proton affinities lower than H_2O molecules. Secondly, most of the common VOCs have proton affinities larger than H_2O and therefore proton transfer occurs on every collision with rate constants that are well known, having typical values 1.5×10^{-9} $cm^3\ s^{-1} \leqslant k(k_L \text{ or } k_{ADO}) \leqslant 4 \times 10^{-9}\ cm^3\ s^{-1}$. An additional advantage of using primary H_3O^+ ions is that many of their proton transfer processes are non-dissociative so that only one product ion species occurs for each neutral reactant. In cases where dissociation does occur they frequently follow a straightforward pattern, *e.g.* the ejection of a water molecule from protonated alcohols and protonated aldehydes.[5]

PTR–MS has been used so far to measure concentrations of benzene and acetonitrile in human breath at levels of a few ppbv[5] and garlic breath has been investigated for compounds such as diallyl sulfide, allyl methyl sulfide, diallyl disulfide, diallyl trisulfide and others,[6] These compounds are present in normal human breath at mixing ratios of a few ppbv, changing significantly after ingestion of garlic. These kind of data provided information on metabolic processes in the body, inferring that garlic compounds enhance fat metabolism, which is just one of the many positive medical effects of garlic. PTR–MS has been used to demonstrate that isoprene in the breath of children is present at much lower concentrations than in adults.[7]

Werner Lindinger, born 1944 in Brixlegg, Tirol, received his PhD at the University of Innsbruck. In 1993–1995 he was working at NOAA, Boulder under the supervision of Professor Eldon Ferguson. Since his return to the University of Innsbruck, where he was appointed as Professor of Physics, he has been investigating ion-molecule-reactions and their application to trace gas analysis, which resulted in the development of proton-transfer-reaction mass-spectrometry, the subject of the above article. He has also held Visiting Professor positions at the University of Utah, Salt Lake City and at the University at Trento, Italy and received the Schrödinger Prize 1997 of the Austrian Academy of Science.

Armin Hansel, born 1962 in Kufstein, Tirol, is Assistant Professor at the University of Innsbruck where he obtained his PhD in 1992. He was a post-doctoral fellow at the Academy of Sciences of the Czech Republic in 1992. He has been involved in the development of proton-transfer-reaction mass-spectrometry and his research interests are ion-molecule-reactions and their application to the analysis of environmentally important trace gases.

Werner Lindinger



Alfons Jordan

Armin Hansel

Alfons Jordan was born in Hall, Tirol in 1963, and he received his PhD at the University of Innsbruck in 1995 where he presently is a research fellow working with Professor Werner Lindinger. He was involved in the development of proton-transfer-reaction mass-spectrometry (PTR-MS) and his research interests lie in trace gas analysis in food chemistry and the further development of PTR-MS.

In the head space air above meat, concentrations of methanethiol and dimethyl sulfide were measured at levels of about 1 ppbv and aromatic compounds in an urban environment were detected at mixing ratios of a few ppbv.[8] Several of these results will be discussed below.

In order to use PTR–MS for on-line monitoring of VOCs in rural ambient air and during flight missions up to 13 km in altitude, where hydrocarbons and oxyhydrocarbons (having mixing ratios in the range of 10 pptv to a few ppbv) play an important role in tropospheric chemistry, we have improved the detection limit of the system so that now compounds can be monitored at levels of a few pptv.[9]

2 The proton-transfer-reaction mass spectrometer (PTR–MS)

In a PTR–MS system (a schematic diagram is shown in Fig. 1)

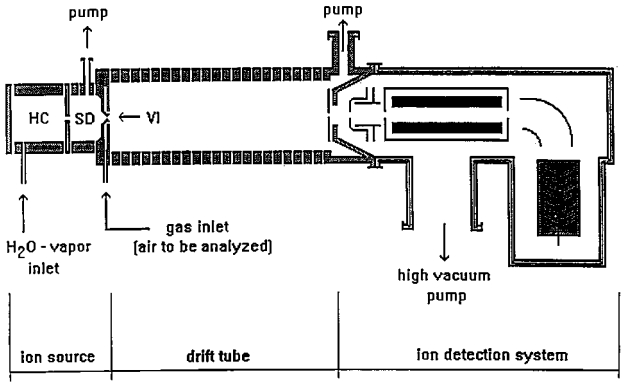


Fig. 1 Schematic representation of the PTR–MS apparatus. HC, hollow-cathode; SD, source drift region; VI, Venturi-type inlet.

primary ions, H_3O^+, react with neutrals under well defined conditions. This is assured by allowing the H_3O^+ reactions to proceed within a flow-drift tube. Details about different types of swarm experiments which also include flow-drift tubes have been discussed in several review articles.[10,11] Usually in drift experiments, primary ions, A^+, travel through a buffer gas B within the drift tube to which the reactant gas R is added. On the way through the reaction region the ions perform many non-reactive collisions with buffer gas atoms or molecules thus being kinetically thermalized. However, once they collide with a reactant gas particle they may undergo reaction (1).

$$A^+ + R \rightarrow \text{products} \quad (1)$$

In the case of H_3O^+, these perform proton transfer reaction (2) (if energetically allowed).

$$H_3O^+ + R \xrightarrow{k} RH^+ + H_2O \quad (2)$$

If only trace components reacting with H_3O^+ are present, the H_3O^+ ion signal does not decline significantly. Therefore, by analogy with the detailed description in Refs. 10 and 11, at the end of the reaction section the density of product ions $[RH^+]$ is given by eqn. (3).

$$[RH^+] = [H_3O^+]_o (1 - e^{-k[R]t}) \approx [H_3O^+]_0 [R]kt \quad (3)$$

Here, $[H_3O^+]_o$ denotes the density of H_3O^+ ions at the end of the drift tube in the absence of reactant neutrals in the buffer gas, k is the reaction rate constant for the proton transfer reaction (2), t is the average time or 'reaction time' the ions spend in the reaction region. As [R] stands for small densities of trace constituents, then $[RH^+] \ll [H_3O^+] \approx [H_3O^+]_o$ = constant. The ion detection system measures count rates $i(H_3O^+)$ and $i(RH^+)$, which are proportional to the respective densities of these ions.

To reach a high sensitivity requires generating a high ion count rate $i(RH^+)$ per unit density [R] in the gas to be analyzed. This obviously can be achieved by keeping the density of $[H_3O^+]$ high by not diluting the gas to be analyzed in an additional buffer gas but by using the air itself (which contains the trace constituents to be analyzed) as the buffer gas. This can be done when H_3O^+ ions are used because they do not react with the natural components of air. A high density of primary ions, H_3O^+, is provided by means of a hollow-cathode ion source. The specific ion source[12,13] used provides H_3O^+ ions with a purity of about 99.5% or better. This situation has two advantages. High concentrations and therefore high count rates of primary H_3O^+ ions are obtained in the ion detection system (typical count rates are $\sim 10^6$ counts s^{-1}) and no quadrupole system needs to be installed to preselect the reactant ions H_3O^+ before entering the reaction region of the system. Besides insignificant traces of NO^+ the only impurity ions of importance (less than 0.5%) are O_2^+ ions, which are produced within the 'source drift region' due to the charge transfer from H_2O^+ ions to O_2 effusing from the reaction region towards the ion source system, or by direct electron impact ionization of O_2. As O_2^+ does not react with H_2O in binary collisions[14] it is not converted into another ionic form once it is produced in an H_2O environment. In contrast, N_2^+ or N^+ ions are rapidly converted into H_3O^+ by multiple collisions with H_2O molecules in the reaction region. From the hollow-cathode source, ions are extracted and after passing a short 'source drift region', they reach an extended reaction region. This is in the form of a drift section of 22 cm length and 5 cm inner diameter through which the air is flowing continuously (pressure a few Torr) and which contains the trace gases to be analyzed. No further buffer gas is needed and therefore the original mole fraction of R in the air is retained in the reaction region. On the way from the Venturi-type inlet to the downstream end of the drift section, H_3O^+ ions undergo non-reactive collisions with any of the common components in air and a small fraction (typically in the order of a few percent) react with trace constituents.

The reaction time t in eqn. (3) which is typically 10^{-4} s can be measured directly, either by pulsing the ions at the entrance and at the exit of the drift tube and monitoring the arrival time spectrum, or by calculating it from mobility values, μ, of H_3O^+ in air, reported in the literature.[15]

Details about the identification of molecules of the same mass, which is often a problem, are discussed by Hansel *et al.*[4] and in a recent review by Lindinger *et al.*[16]

When H_2O is used as the discharge gas in a hollow-cathode ion source, due to fortuitous ion-molecule-reaction sequences, only H_3O^+ ions (with a few other traces) are extracted.[4] Similarly, when NH_3 is in the hollow-cathode, only NH_4^+ ions emerge from the source, and can thus be used as primary reactant ions. Whilst H_3O^+ ions perform proton transfer to all VOCs having a proton affinity (PA) higher than 166.5 kcal mol^{-1}, NH_4^+ only performs proton transfer to compounds with PAs in excess of 204 kcal mol^{-1}. When air containing traces of pinene and 2-ethyl-3,5-dimethylpyrazene, both having a molecular mass of 136 Dalton is analyzed using H_3O^+ ions, the product ion signal at mass 137 will partly originate from pinene (pinene, PA < 204 kcal mol^{-1} forms fragment ions upon protonation from H_3O^+, but about 20% of the product ion is non-dissociated protonated pinene) and partly from 2-ethyl-3,5-dimethylpyrazene (PA > 204 kcal mol^{-1}). If NH_4^+ is then used as a primary reactant ion, the ion signal at mass 137 only can originate from 2-ethyl-3,5-dimethylpyrazene.

With these methods identification of compounds can, in many cases, be ascertained unambigously, however we still want to emphasize that the primary strength of PTR–MS is in the monitoring of compounds, rather than for compound analysis.

3 Applications

In this section we present a selection of results obtained in different fields of research such as medical applications, food control and environmental research.

3.1 Medical applications *via* breath analysis

Exhaled human breath contains the natural constituents of air and also a variety of endogenous volatile organic compounds. The most abundant ones of these are acetone, methanol, ethanol, propanol and isoprene. Acetone is normally present in concentrations of ~1 ppmv while the others have concentrations of typically one hundred to a few hundred ppbv. Besides these abundant compounds there are concentrations of a few ppbv of other compounds, such as benzene, acetonitrile and diallyl sulfide, allyl methyl sulfide, diallyl disulfide just to mention a few. These compounds are produced within the human body in metabolic processes. If these processes are influenced by the intake of unusual amounts of specific kinds of food or chemicals, many of the above compounds can show concentrations deviating significantly from the 'normal' values. PTR–MS allows detailed analysis of human breath and it has been applied for on-line monitoring of the fast enzymatic conversion of propan-2-ol into acetone, as well as for metabolic processes due to the ingestion of garlic. Drastic differences in breath isoprene concentrations have been observed between adults and children; the endogenous production of methanol after the consumption of fruit has been measured quantitatively and a detailed analysis was done on acetonitrile and benzene in the breath of smokers and non-smokers. In the following we present a summary of these investigations.

3.1.1 Enzymatic conversion of propan-2-ol into acetone

Oral ingestion of about half a gram of propan-2-ol (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 shows the concentration of acetone in breath

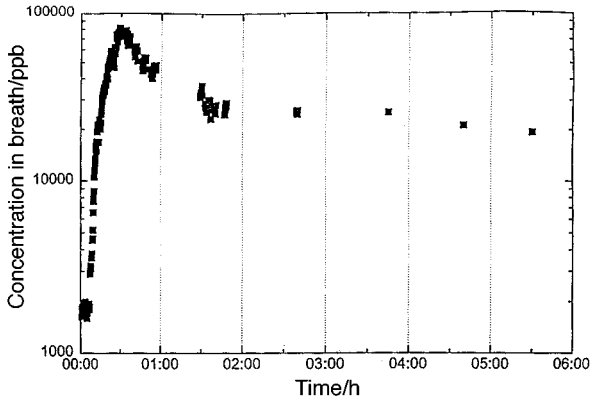


Fig. 2 Concentration of acetone in the breath of a person after consumption of 0.45 g propan-2-ol

measured on-line. About five minutes after the start of the measurements, the propan-2-ol–water mixture was ingested by a test person, and after rinsing of the mouth with pure water, the measurements were continued. An increase of the acetone concentration, finally rising up to ~80 ppm at 30 minutes after the start of the experiment was observed, followed by a slow decline during the next five hours during which time only sporadic measurements were carried out. Due to enzymatic action propan-2-ol is converted into acetone within the stomach and then reabsorbed to reach the blood stream. This process occurs fast enough so that no increase of the propan-2-ol concentration in the breath is observed. In contrast to this, if the same experiment is performed by taking propan-2-ol intravenously, the concentration of propan-2-ol in the breath increases rapidly (see Fig. 3), reaching a maximum within one minute and declining thereafter, whilst acetone increases within about 1–3 minutes by a factor of about 50, staying at this enhanced level for the next few hours. In this case the respective enzyme situated in the liver converts propan-2-ol into acetone, which then takes a long time to be removed from the body. These kind of processes can be used for testing the function of

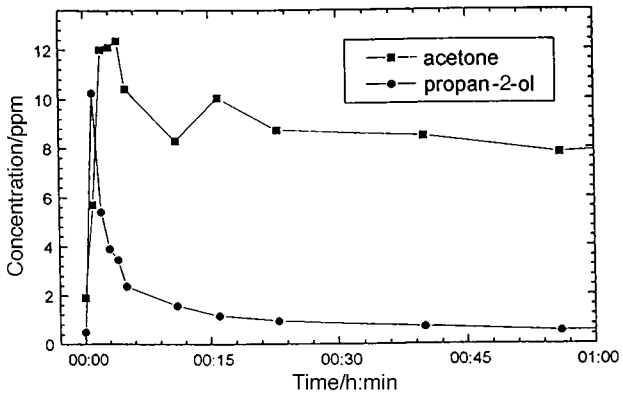


Fig. 3 Concentrations of acetone and propan-2-ol in the breath of a test person after intravenous application of 0.45 ml propan-2-ol (diluted) at time zero

various organs in the body and non-invasive diagnostic methods based on PTR–MS will be developed in the near future.

3.1.2 Garlic breath

Garlic has been used as an important dietary constituent and as a medicine for the treatment of many disorders[17] since ancient times by the Egyptians, Greeks and Romans right up to the present day. Intact garlic *Allium sativum* cloves hardly produce any significant smell, but crushed or cut garlic develops an extremely strong odour which also appears in the breath of persons who have consumed garlic. The strong odour persists for time spans of up to more than a day. The phenomenon is now well understood. Within the garlic cloves odourless alliin is stored in the mesophyll cells, well separated from an enzyme called alliinase, which is situated in the vascular bundle sheath cells. When force acts on the garlic cloves, so that the cells are damaged by crushing or cutting, the enzyme comes in contact with the alliin converting it to allicin which has the typical odour of garlic. Allicin in turn is converted into rather strongly smelling organosulfides (such as diallyl disulfide and others), the chemistry of which has been investigated and described in great detail by Block.[18] Diallyl disulfide is known to inhibit the activitation of nitrosamine, thus reducing the probability of the development of cancer of the stomach. 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 disulfide 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 (Fig. 4). 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. 5). Allyl methyl sulfide reaches a maximum of about 900 ppbv after 4–5 hours, then declines quite slowly such that more than a day later substantial concentrations of 100–250 ppbv are still observed. While allicin is observed in the head space air above 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 Laakso *et al.*[19] that allicin is quite unstable in fatty oil extracts.

Quite remarkable is the observed increase of the acetone concentration (Fig. 5) in the breath of the test person which rose from 1.8 ppm to 5 ppm after 24 hours.[6] Enhanced levels of acetone are observed in people suffering from diabetes. Healthy people show higher concentrations of acetone after fasting for more than 10 to 15 hours or after performing strong exercise for 2 to 3 hours (see Fig. 6). In these cases the human body has fully exploited its sugar reserves in the blood and thus has started

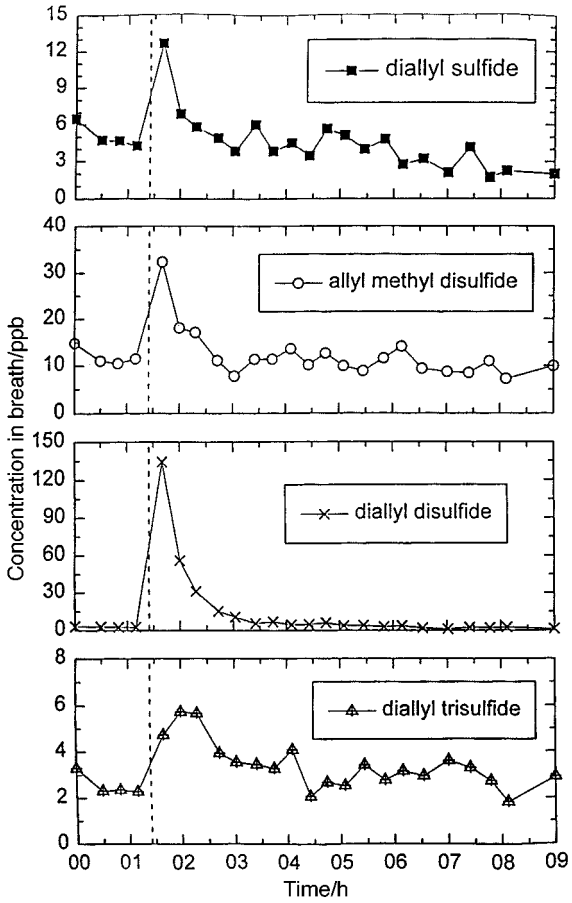


Fig. 4 Variation in the concentrations of diallyl sulfide, allyl methyl disulfide, diallyl disulfide and diallyl trisulfide in human garlic breath with time. The time 00 corresponds to 9:00 a.m. The vertical dashed line indicates the time of ingestion of garlic (from Ref. 6).

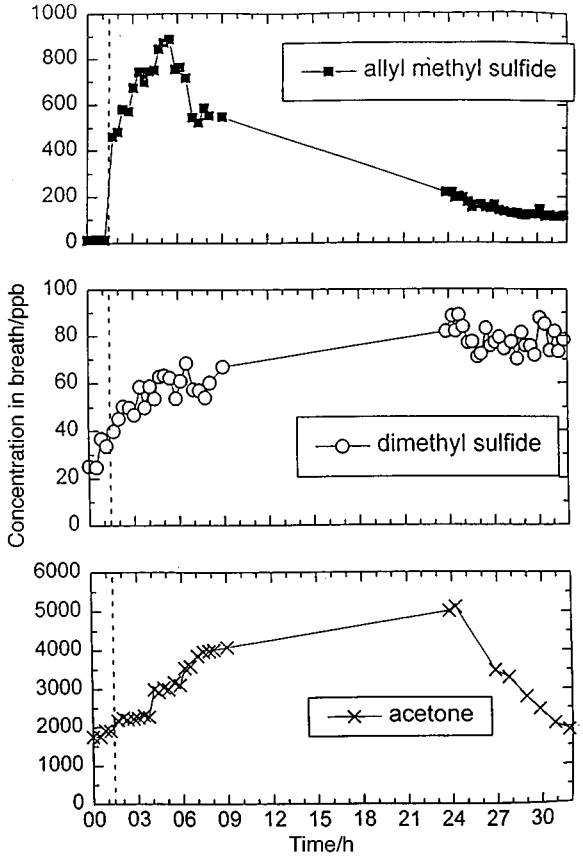


Fig. 5 Variation of allyl methyl sulfide, dimethyl sulfide and acetone in human garlic breath with time. The time 00 corresponds to 9:00 a.m. The vertical dashed line indicates the time of the ingestion of garlic (from Ref. 6).

metabolizing its fat reserves which results in the production of acetone. In this context the observations of Bakhsh and Chughtai[20] are worth noting, that levels of serum cholesterol, serum triglicerydes, 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 observation of enhancement of acetone production after ingestion of garlic (Fig. 5) may be indicative of enhanced metabolism of fatty components in the bloodstream, thus reducing the above-mentioned compounds. In view of these findings it might not be just incidental that in southern European countries, where much more garlic and probably more fat is consumed than in northern countries, coronary diseases and heart attacks are much less common.

3.1.3 Isoprene

The origin of human isoprene is probably related to the isoprenoid biosynthetic pathway, but whether its formation is enzymatic or non-enzymatic is uncertain. It is clearly endogenous in origin[21] most likely as a by-product of the biosynthesis of isoprenoid compounds, their decomposition, or both. Evidence points towards a cellular origin of the isoprene with excretion predominately *via* the lungs resulting from its low water solubility and low boiling point. Deneris *et al.*[22] have demonstrated the *in vitro* synthesis of isoprene from DL-mevalonate. They advanced the hypothesis that breath isoprene is linked to cholesterol biosynthesis, which relies on the mevalonate pathway. Administration of the drug lovastatin, a competitive inhibitor of the mevalonate-forming step of cholesterol biosynthesis in humans, was demonstrated by Stone *et al.*[23] to suppress isoprene in the breath. In addition, cholesterol feeding, which suppresses mevalonate formation, also lowered breath isoprene. These results strongly support the

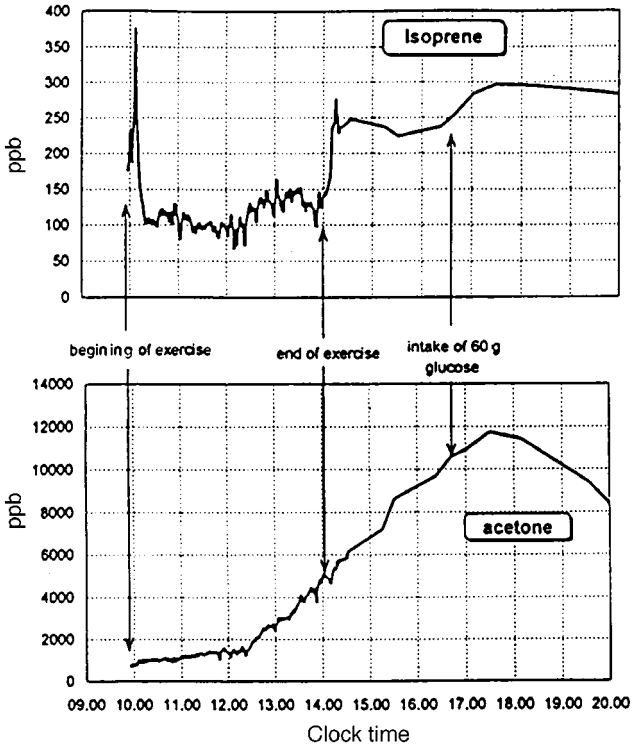


Fig. 6 Concentrations of isoprene and acetone in the breath of a test person starting physical exercise (bicycling) at 10h03 and ending it at ~14h00

hypothesis of Deneris *et al.*[22] Small amounts of breath isoprene might arise from peroxidation of the cholesterol precursor, squalene.

Results obtained in our laboratory[7] provide new information on isoprene levels in exhaled air, its variation between subjects, and as a function of wakefulness for adult subjects and infants. For example, Fig. 7 reports isoprene levels detected in the

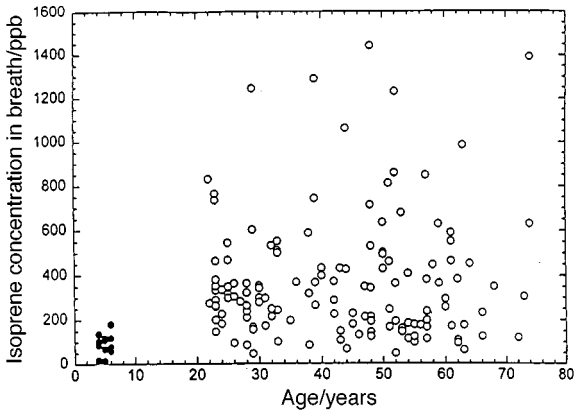


Fig. 7 Concentrations of isoprene in the breath of 158 test persons as dependent on age. All measurements were performed during the daytime (from Ref. 7).

breath of 141 adults and 17 children, all healthy volunteers, using the methods described above. The adults ranged in age from 22–74 years and the children, from 4–6 years. In agreement with Mendis *et al.*[24] we find no evidence for age dependence within the group of adult test persons in Fig. 7. However, the concentration of isoprene in young children is demonstrably lower than in adults as shown clearly in Fig. 7. The average isoprene concentration is 100 ± 50 ppbv, lower by a factor of about 2.4 than in the adult population.

Pronounced diurnal changes in the isoprene concentration in breath was reported by De Master and Nagasawa,[21] peaking between the hours of 02h00 and 07h00 to a level nearly four times greater than their daytime levels. It was later shown by Cailleux and Allain that this diurnal variation is associated with the state of sleep and wakefulness rather than an intrinsic circadian rhythm.[25] We have also investigated this phenomenon.[7] In agreement with previous results, we find an increase by a factor of 2–4 in isoprene during the night for the adult participants in our study. However, these observed diurnal variations of the isoprene concentrations do not necessarily indicate diurnal changes of the endogenous production of isoprene. This can be explained by means of the isoprene data shown in Fig. 6. Before the start of physical exercise the test person had a breath isoprene concentration of about 200 to 220 ppb. A few minutes after the start of the exercise the isoprene concentration rose to a maximum of ~370 ppb and a few minutes later it had dropped to ~100 ppb, remaining there during the total time span of the exercise. When the exercise was stopped the breath isoprene concentration rose to values similar to those before the exercise had begun and stayed there with small variations for the next few hours.

At first sight one might be tempted to interpret the variation of the isoprene concentration as indicative of the variation of endogenous isoprene production in the body of the test person. This is not the case. The isoprene source was to a first degree constant over the whole time period investigated: isoprene has a low solubility, *i.e.* it has a small Henry's law constant. This means that the human body is an inefficient buffer for isoprene. Isoprene produced in the body is transported *via* the blood stream to the lungs where it evaporates quite efficiently and the actual concentration of the isoprene in the breath is governed by the production term (which is constant) and by the velocity of the blood stream pumped through the lungs (which is proportional to the heart beat frequency) and the breathing rate. Before the exercise begins the test person has a typical heart beat rate of about 60–70 min^{-1} and the usual breathing rate. As soon as the exercise is started the heart beat rate increases within seconds, reaching about 120 min^{-1} within the next few minutes. During this period blood is pumped at a higher speed through the lungs and more isoprene evaporates through the lungs. As during this initial period of the exercise the breathing rate has not yet changed, this results in a higher concentration of isoprene in the breath, and we observe the initial peak of about 370 ppb (Fig. 6). As the source of isoprene stays constant the enhanced rate of evaporation leads to a decline in the blood isoprene concentration and thus of the evaporation rate. In addition, after a few minutes the breathing rate increases, leading to an enhanced dilution of the isoprene, again resulting in a decline of the breath isoprene concentration. After 10 to 15 minutes the body of the test person has reached a steady state with an enhanced heart beat rate of about 115 min^{-1} and a doubling of the breath rate as compared to normal. If only the heart beat rate were enhanced, but not the breath rate, the concentration of isoprene in the breath would be the same as before the start of the exercise. The lower concentration of isoprene in the blood would be compensated for by the higher evaporation rate within the lungs due to the enhanced heart beat rate. But due to the enhanced breath rate the isoprene concentration is lowered inversely proportional to the breath rate. This situation remains until the exercise is ended, after which the breath rate and heart beat rate again reach values similar to those before the exercise had started, and therefore also the isoprene concentration in the breath becomes similar to that before the start of the experiment. Thus the observed strong variations in the breath isoprene concentration (Fig. 6) are well explained on the basis of constant endogenous isoprene production.

Similarly the observed diurnal variations of the breath isoprene concentration with maxima during the night can be explained on the basis of a (nearly) constant endogenous isoprene production. During the night the average breath rate is somewhat lowered, thus resulting in an enhanced breath isoprene concentration. Furthermore the heart beat rate is also lowered during the night, resulting in an enhanced blood isoprene concentration. However, as soon as a test person wakes up due to an alarm signal and moves in order to inflate a test bag, the heart beat rate immediately increases which results in an overall increase of the breath isoprene concentration which is explained in the same fashion as the initial increase observed at the beginning of the physical exercise described above (Fig. 6). The first quantitative measurements on heart beat and breath rates of test persons involved in investigations of the diurnal variation of the breath isoprene concentration confirm this hypothesis. Conclusively, these results infer that the observed time dependent variations in breath isoprene concentrations are not indicative of a connection between endogenous isoprene production and the sleep or wakefullness of a person.

3.1.4 Endogenous production of methanol

Even if a person does not drink any alcoholic beverages at all, an individual's blood shows a natural, physiological ethanol and methanol level, the origin of which is not yet definitely identified. A typical human body produces up to 30 g of ethanol per day and 0.3 to 0.6 g methanol per day resulting in concentrations of ethanol and methanol in the blood of typically 0.2 to 0.8 mg l^{-1} and 0.5 mg l^{-1}, respectively.[26] These values correspond to 0.05 to 0.20 ppm of ethanol and 0.15 to 0.6 ppm of methanol, respectively in the breath. After the consumption of fruit the concentration of methanol in the human body increases by as much as an order of magnitude. This is due to the degradation of natural pectin in the human colon by bacteria. *In vivo* tests were recently performed by means of PTR–MS in order to obtain quantitative information on this endogenous production of methanol.

We were interested in measuring quantitatively the release of methanol in the human body after the consumption of fruit.[27] The baseline concentration of methanol in the body reflects a balance between endogenous production and metabolic loss. It has been well established that the metabolic loss of methanol is completely stopped when the human body contains an elevated concentration of ethanol. This allows the measurement of the

endogenous baseline methanol production to be typically 0.28 mg l^{-1} h^{-1} or about 0.3 g day^{-1} for a 70 kg man. This same technique may be used to measure methanol production when fruit is consumed because the methanol production is even greater. These measurements have been made for different kinds of fruit and on pure pectin. One example of data is shown in Fig. 8. Four test persons were given 75 g each of a mixture of

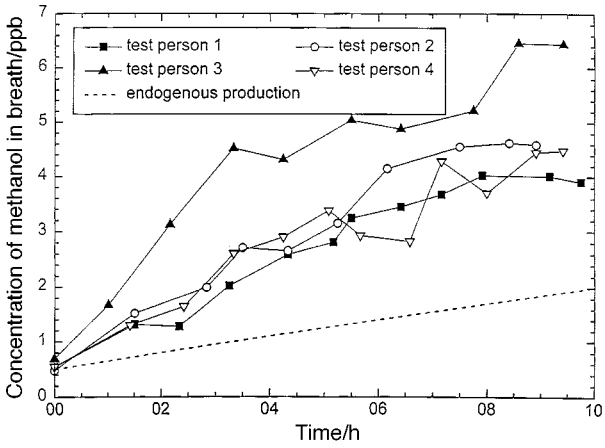


Fig. 8 Increase of the concentration of methanol in the breath of four test persons after consumption of 1 kg apples each at time 0. Over the whole time period of the experiment, ethanol concentration in the blood was kept in excess of 150 mg l^{-1} (from Ref. 27).

pure ethanol and distilled water (40/60%) at the beginning of the experiment, and again 2.5 hours later, in order to maintain an ethanol concentration in the breath above 40 ppmv, and thus in the blood well in excess of 150 mg l^{-1} throughout the 51/2 hours of the duration of the experiment. The methanol concentration (as well as that of ethanol) in the breath of the test persons was measured by PTR–MS at intervals of approximately 30 minutes.

The initially measured concentrations of 0.25 to 0.35 ppmv respectively are typical base methanol concentrations, but due to the intake of ethanol by the test persons right at the beginning of the experiment, the now enhanced ethanol concentration in the body inhibited methanol metabolism, thus causing an increase of the breath methanol concentrations as a function of time, as shown by the dashed line (representing the averaged data) in Fig. 8. The graph yields a value for the increase of the methanol concentration of 0.15 ppmv h^{-1} which corresponds to about 0.6 g day^{-1}, and is in fair agreement with the findings of Gilg *et al* .[26] mentioned earlier.

Several days later the identical four test persons performed the same experiment with the only exception that now they additionally ate ~1 kg of apples each at the beginning of the experiment. Apples typically contain ~1% pectin, with a degree of methylization of ~75%. Thus, a typical quantity of ~1.3 g of methanol is contained in the pectin of the 1 kg apples consumed. Again the methanol (and ethanol) concentrations in the breath of the test persons was measured throughout the duration of the experiment for ~10 hours.

The respective amount of methanol released, as calculated from the measured breath methanol concentration shown in Fig. 8, is approximately 32–56% of the total amount of methanol bound in the pectin of the consumed apples. Additional measurements performed with 6 test persons yielded fractions of methanol released between 25 and 52%. The final statistics, including data from all 10 persons tested, show a release of 40 ± 9% of the methanol contained in the consumed apples. Here the main uncertainty lies in the content of ~1% of pectin in the apples, which is subject to an uncertainty of ± 50%. Therefore we may assume that between 20% and 100% of all the methanol contained in the pectin of the consumed apples is finally reabsorbed in the body. These results show that after the consumption of fruit, the methanol bound in the fruit pectin is released quantitatively and transferred to the blood. Thus after consumption of 1 kg of apples, a total of typically 0.5 g of methanol is released in the human body. Therefore the daily consumption of a few apples or oranges increases the endogenous production of methanol over the normal rate (this being 0.3 to 0.6 g day^{-1}) by about a factor of two. To acquire the same quantity of methanol, a person would have to drink 0.3 litres of brandy (40% ethanol) containing 0.5% of methanol (as compared to the ethanol content). This would qualify as significantly methanol-contaminated liquor!

3.2 Food research

Monitoring the emission of VOCs can be used for control of the ripening/aging processes of fruit, and thus on the development of their aroma patterns.[16] Also the onset of the degradation of meat can be recognised: in the summer there is often the danger that any kind of meat which is not stored properly at a low enough temperature may deteriorate to a degree where it should no longer be consumed. VOC emissions associated with microbial growth are indicative of the degree of deterioration.[28] PTR–MS provides a simple and fast working tool for controlling the state of meat. Fig. 9 shows the emission of various

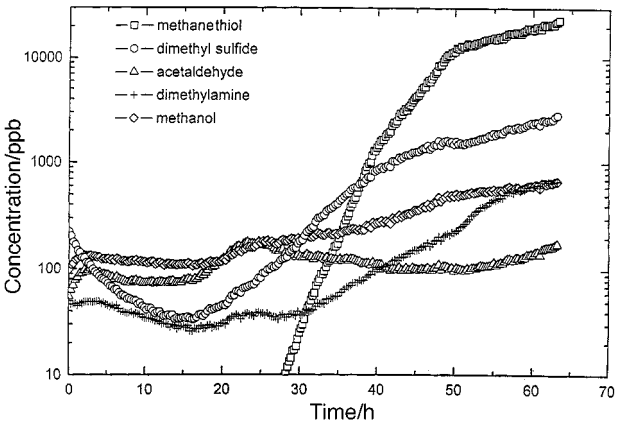


Fig. 9 Concentrations as dependent on time of various compounds in the head space of beef meat kept at 22 °C

compounds from a sample of meat purchased from a local supermarket and then kept at room temperature for about 63 hours. The data show a significant increase of methanethiol from a few ppbv at 27 h to more than 2000 ppbv at 60 h. Dimethyl sulfide increases less strongly than methanethiol. Usually meat is still consumable as long as the concentration of methanethiol is well below that of dimethyl sulfide. It is obvious that the head space concentrations of the compounds in Fig. 9 are a clear indicator of the degree of freshness or degradation of the meat. PTR–MS tests are especially useful as they can be performed within a few minutes, while results of bacteriological tests are available only after several days.

3.3 Environmental applications

3.3.1 Emissions of partially oxidized volatile organic compounds (POVOCs) from dead plant material to the atmosphere

Plants emit a wide variety of organic compounds, including isoprene, terpenes and oxygenated compounds, which form an important contribution to the global budget of non-methane hydrocarbons. While emission inventories for living plants are being improved,[29] hardly any effort has been made to investigate the potential emission from decaying biomaterial. This is surprising in view of the fact that about 6–8 $\times$ 10^{16} g of leaf biomass are decaying each year on earth.

Recently we performed PTR–MS investigations[30] which yielded the first data which allow preliminary estimates of the release of POVOCs from decaying biomaterial, based both on laboratory experiments and some preliminary field work.

From applications in the food industry it is well known that heating of biomaterial leads to the formation of POVOCs due to non-enzymatic thermochemical reactions. The most outstanding example of this is in the roasting of coffee in which high

temperatures yield a favourable combination of POVOCs with a pleasant aroma pattern. Any other decaying biomaterial, such as leaves, grass or needles, also forms a variety of POVOCs, with the rate of formation strongly dependent upon temperature. However, even at room temperature considerable amounts of POVOCs are produced over time periods of days and weeks and amongst the most abundant components are acetone, acetaldehyde, methanol, ethanol, acetic acid and other compounds which are also found in roasted coffee.

An interesting feature of the production of POVOCs in decaying biomatter is the fact that their rates of production are usually not proportional to their rates of release to the air. As in coffee, POVOCs produced by roasting initially remain attached to the cell material of the biomatter due to their polarizability. Even if we grind roasted coffee beans, the release rate of POVOCs from dry coffee powder is relatively low. However, after water is added to the coffee powder, strong emissions of aroma compounds occur. The highly polar water molecules replace the POVOC molecules attached to the cell material and the POVOCs dissolve in the water. The resulting coffee brew is a mixture of ideal-dilute solutions of POVOCs in water and the partial pressures of the POVOCs in the gas phase in contact with the liquid tend towards values that are governed by Henry's law. In this way POVOCs are released over time, establishing the well known aroma of a cup of coffee. For illustration of the above, we present the data in Fig. 10 showing the head space

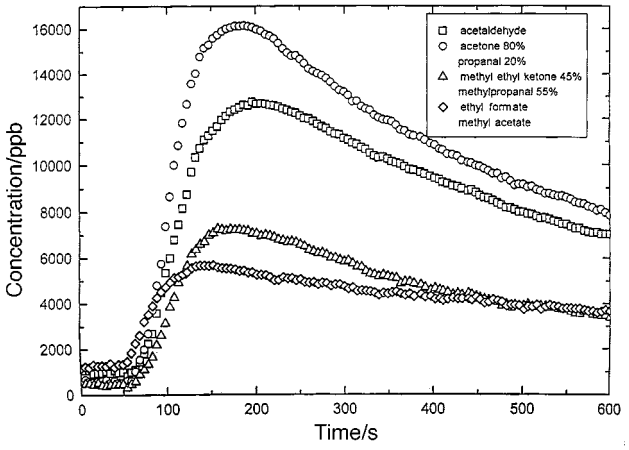


Fig. 10 Concentration as dependent on time of acetaldehyde, acetone (80%) plus propanal (20%), methyl ethyl ketone (45%) plus methylpropanal (55%) and ethyl formate plus methyl acetate in the head space of 2 g freshly ground coffee to which, after 50 sec, 90 g water (17 °C) was added

concentrations of various POVOCs above 2 g of dry, freshly ground coffee powder (0 to 50 sec) to which after 50 sec, 90 g of water (at a temperature of 17 °C) was added. The same holds true for coffee as for any biomaterial, such as leaves or needles, that has been kept at given temperatures for some time during which the POVOCs are produced at a rate which depends on temperature. As long as the biomaterial is kept dry the rate of POVOC release is quite low. Here also, when water is added, the POVOCs within the biomaterial dissolve in the water and are released to the head space according to Henry's law. It is in this way that after a hot summer day, when the first drops of a rainstorm fall onto the ground of a meadow or a forest, a strong smell is produced. The same occurs after a hot day, when, during the night, a dew forms bringing moisture to the biomaterial on the ground.

We have used a combination of heating/wetting cycles to estimate the total POVOC release rates to the atmosphere.[30] These data, obtained from a variety of biomaterials, show that the relative emission of acetone and methanol can be at least 10^{-4} and 3–5 $\times$ 10^{-4} grams per gram of decaying dry plant matter, respectively. If these results may be extrapolated, global annual emissions of 6–8 Tg of acetone and 18–40 Tg of methanol would result, adding strongly to the estimated total emissions of these compounds to the atmosphere.

Acetone plays a substantial atmospheric photochemical role, both as a source of $HO_2^{\bullet}$ radicals in the upper troposphere and as an intermediate sink of NO_x *via* the production of PAN.[31] Methanol oxidation is a source of formaldehyde. As the photochemical decay of CH_2O in the atmosphere leads to production of $2HO_2^{\bullet}$ radicals, methanol may also play a role in the atmospheric HO_x budget.

3.3.2 Volatile organic compounds in ambient air: demonstration of the detection limits of PTR–MS of a few pptv

The present status of the detection limits of PTR–MS is best demonstrated by the following data on the diurnal variations in air of components originating from traffic. Fig. 11 shows data

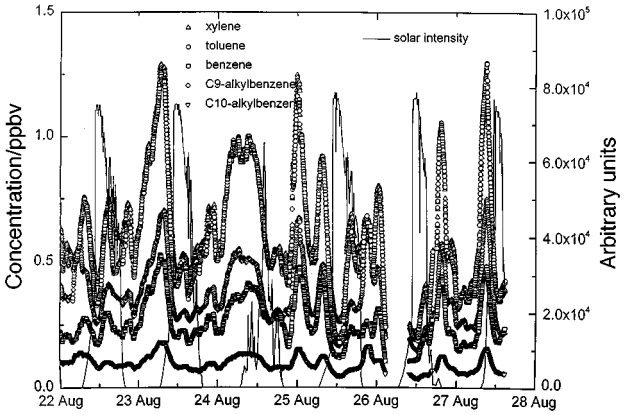


Fig. 11 Diurnal variations of the concentrations of compounds as indicated, in the atmosphere at the western outskirts of Innsbruck (left hand scale), and solar radiation intensity (right hand scale, arbitrary units) as measured from August 22nd–August 27th, 1997 (from Ref. 9)

for benzene, toluene, xylene C9- and C10-alkylbenzenes obtained during the time period from 0h00 August 22nd until 14h40 on August 27th (with a few interruptions) at the western outskirts of Innsbruck.[9] At the same time data were taken for an additional 25 compounds which are not shown. Sampling times ranged from 3 to 10 sec per mass, so that every 21/2 min a set of data was obtained. The data shown in Fig. 11 represent the running means of 50 data points, and represent the total sum of xylene C9- and C10-alkylbenzenes respectively. The relative concentrations of these compounds are in agreement with a variety of reported values in the literature for 'low photochemical age', *i.e.* the concentrations of toluene and xylene are higher by a factor of 2 to 3 than the ones for benzene. The concentrations of C9-alkylbenzenes are comparable to benzene and the ones of C10-alkylbenzene are significantly lower than those of benzene. The ratios of the densities of these compounds are approximately constant over the whole time period of the measurements, indicating that all these aromatic compounds originate from the same sources, mainly the burning of fossil fuels.

Fig. 12 represents the data for C9-alkylbenzene (in its protonated form at mass 121), together with the simultaneously measured concentrations of the ^{13}C-isotope of C9-alkylbenzene (in its protonated form at mass 122). The natural ratio of parent C9-alkylbenzene to its ^{13}C-isotope is 9.75. A correlation plot of all the measured intensities (measured from August 22nd to August 28th) for mass 121 *versus* those for mass 122, yields a ratio of 9.70 which is in good agreement with the calculated value of 9.75. This finding shows that the compound at mass 122 (typical value at night, 50 pptv) originates *mainly* from the ^{13}C-isotope of C9-alkybenzene and does not include significant amounts (about 2 pptv at night) of other compounds of the same mass. Furthermore we see from Fig. 12 that time dependent changes of even less than 10% in the mass 121 signal are well reproduced in the mass 122 signal. At total concentrations of about 50 pptv of the ^{13}C-isotope of C9-alkylbenzene this indicates that PTR–MS has a sensitivity of about 5 pptv for these kind of compounds.[9]

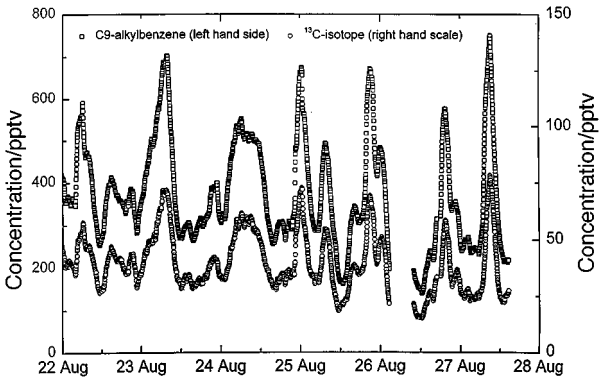


Fig. 12 Diurnal variation of the concentration of C9-alkylbenzene and of its ^{13}C-isotope in the atmosphere at the western outskirts of Innsbruck as measured from August 22nd–August 27th, 1997. The left hand scale pertains to the parent compound, the right hand scale to its ^{13}C-isotope (from Ref. 9).

The most spectacular measurements so far carried out were done by monitoring a variety of VOCs during the LBA–CLAIRE (Cooperative Large Scale Biosphere Atmosphere Airborne Regional Experiment) campaign in March 1998 in the Amazonas region. Fig. 13 represents the first results on the

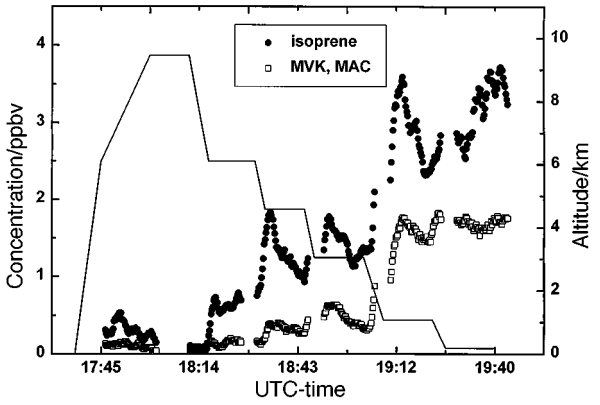


Fig. 13 Concentrations of isoprene as well as of methyl vinyl ketone (MVK) plus methacrolein (MAC), measured on-line during a flight above the Amazonas region in March 1998 as part of LBA-CLAIRE

densities of isoprene as well as on the sum of methyl vinyl ketone (MVK) and methacrolein (MAC) measured on-line, together with many other compounds, during the flight of a Cessna Citation.[32] Also shown in the Figure is the cruising altitude of the aeroplane. The data clearly indicate a strong decline of the concentrations of the above mentioned compounds as the altitude increases, as is expected from short lived VOCs in the troposphere. These data will be used for model calculations of tropospheric chemistry.

4 Conclusion

The applicability of PTR–MS for on-line measurements of trace constituents has been demonstrated by examples in the field of medicine, food control and environmental research. Further exploitation of the method will be: non-invasive medical diagnostics, investigations of metabolic processes and drug detection as well as monitoring of VOC emissions from industrial plants and especially on-line process monitoring of industrial fermentation and food production processes. Promising applications will also be the monitoring of catalytic processes and of material production in plasma reactors. The high sensitivity of the system which has now been reached allows for continuous emission control and monitoring of VOCs in urban and also clean rural environments.

5 Acknowledgements

The development of PTR–MS was made possible due to support from Fa. Nestle (Nestec Ltd., Switzerland) and from GSF-Forschungszentrum für Umwelt und Gesundheit (Neuherberg, Germany). Most recently we also obtained support from Fonds zur Förderung der wissenschaftlichen Forschung under Project P 12022.

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Received 5th November 1997
Accepted 20th May 1998