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Hot-work performed on polyurethane (PUR) coated materials can result in thermal decomposition of the PUR layer subjected to heat. Isocyanates are among the decomposition products. During hot-work the generation of heat is often variable, thus the decomposition products will occur as short-lived peak exposure events. These peak exposure events can be challenging to measure using time-averaged indirect sampling methods. Proton transfer reaction-mass spectrometry (PTR-MS) can offer real-time continuous data recording with high selectivity and sensitivity. This study presents the use of PTR-MS for the real-time quantitative measurement of isocyanic acid.

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PAPER

# The applicability of proton transfer reaction-mass spectrometry (PTR-MS) for determination of isocyanic acid (ICA) in work room atmospheres

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A method is presented for the real-time quantitative determination of isocyanic acid (ICA) in air using proton transfer reaction-mass spectrometry (PTR-MS). Quantum mechanical calculations were performed to establish the ion-polar molecule reaction rate of ICA and other isocyanates. The PTR-MS was calibrated against different ICA air concentrations and humidity conditions using Fourier transform-infrared spectroscopy (FT-IR) as quantitative reference. Based on these experiments a simple humidity dependant model was derived for correction of the PTR-MS response for ICA. The corrected PTR-MS data was linearly correlated ($R^2 > 0.99$) with the data acquired by FT-IR. The PTR-MS instrumental limit of detection (LOD) for ICA was 2.3 ppb. Humid atmospheres resulted in LODs of 3.4 and 7.8 ppb, at an absolute humidity (AH) of 4.0 and 15.5 g $m^{-3}$, respectively. Furthermore, off-line sampling using denuder and impinger samplers using di-n-butylamine (DBA) as derivatization reagent was compared with PTR-MS measurements in a dynamically generated standard ICA atmosphere. Denuder (*n* = 4) and impinger (*n* = 4) sampling subsequent to liquid chromatography mass spectrometry (LC-MS) determination compared to corrected PTR-MS data resulted in recoveries of 79.6 (8.1 % RSD) and 99.9 (9.3 % RSD) %, respectively. Measurements of ICA from thermally decomposed cured 1,6-hexamethylene diisocyanate (HDI)-paint was performed used PTR-MS and denuder (*n* = 3) sampling. The relation between the average ICA responses using denuders (34.4 ppb) and PTR-MS (42.6 ppb) was 80.6 %, which coincided well with the relative recovery obtained from the controlled laboratory experiments using dynamically generated ICA atmospheres (79.6 %). The variability in ICA air concentration during the welding process (170 % $RSD_{PTR\text{-}MS}$) illustrated the need for real-time measurements.

## Introduction

Polyurethanes (PUR), which are reaction products of diisocyanates and polyols, are versatile polymers that are used in a multitude of applications. The chemical bond between an isocyanate and a polyol in PUR products is not thermally stable, and can potentially be broken upon treatment at elevated temperatures to release compounds containing isocyanate or amino groups, such as the diisocyanate building bricks of the polymer and the aliphatic monoisocyanate methyl isocyanate (MIC) and isocyanic acid (ICA).[1] Studies have shown that thermally decomposing PUR and epoxy resins emit ICA in larger amounts than other isocyanates.[2-4] Thus, hot work on PUR-coated metal surfaces, as well as metal forging, may pose a risk of ICA and isocyanate exposure to workers.

Diisocyanates are highly toxic substances that act as respiratory and skin irritants[5, 6] and respiratory sensitizers[7] with the possibility of inducing asthma and hypersensitivity pneumonitis (HP).[8] Furthermore, isocyanates have mutagenic potential through their ready reaction with DNA to form adducts.[9] The acute toxicity potential of MIC at high doses is well known, while the health effects from short-term occupational exposure primarily cause eye and mucous membrane irritations. However, a relationship between occupational exposure to MIC and chronic health effects is not established.[1] Health risks in relation to occupational ICA exposure are to the authors' knowledge not described in the literature and there exist no published data on the toxicology of ICA.[10] Nevertheless, there are concerns regarding occupational exposures to thermal decomposition of PUR products, such as ICA, and adverse health effects. And there is a need for adequate and well-documented analytical methodology suitable for exposure characterization and assessment of such thermally released decomposition products.

Measurements of airborne isocyanates are traditionally done by personal pumped air sampling, followed by chromatographic analyses in the laboratory of desorbed solutes. The isocyanates are collected by either use of filter cassettes, impingers or sampling tubes, through a derivatizing process where the isocyanates are reacted with a nucleophilic agent (usually an amine) due to their unstable nature.[8, 11] Diffusive sampling has also been developed.[12-14]

These methods collect air samples over a given timeframe, normally minutes to hours, resulting in time-averaged measurements. Processes involving thermal decomposition will usually result in transient peaks of decomposition products, which can be challenging to measure with indirect time-averaged methods due to the short time span of the peak exposure events. One way to measure peak exposure values is to reduce the sampling time, which in turn will increase the detection limit of the method.

A more attractive approach might be the use of direct-reading instruments which can provide real-time continuous data recording and thus are more applicable for transient peak exposure measurements. Real-time detection of volatile organic compounds (VOCs) can be provided by commercially available monitors. They rely mainly on infrared (IR), flame ionization detection (FID) or photo ionization detection (PID).[15] However, these techniques have limited selectivity and are thus not suitable for quantitative measurement of e.g. ICA in complex workroom atmospheres which require technology yielding a selective signal related to the component of interest.

Proton transfer reaction-mass spectrometry (PTR-MS) is a technique which provides real-time data with high selectivity and sensitivity of airborne components in gaseous or vapour phase. PTR-MS is a fairly novel technique, which is described in detail elsewhere,[16-20] employing chemical ionization by means of $H_3O^+$ ions produced from water vapour plasma. The $H_3O^+$ ions are transferred to an evacuated drift tube where they may collide with a trace compound *R* and result in a proton transfer reaction, given that the trace compound *R* possesses a proton affinity (PA) higher than that of $H_2O$ (690.4 kJ mol$^{-1}$):[21]

$$H_3O^+ + R \xrightarrow{k} RH^+ + H_2O \qquad (1)$$

If $[RH^+] << [H_3O^+]$, then the density of the protonated analyte $RH^+$ is given by

$$\left[RH^+\right] = \left[H_3O^+\right]_0 \left(1-e^{-k[R]t}\right) \approx \left[H_3O^+\right]_0 [R]kt \qquad (2)$$

where $[H_3O^+]_0$ is the density of the primary ion with the absence of *R*, *k* is the proton-transfer rate coefficient and *t* is the time spent by the primary ion to traverse the drift tube.

The ionization in PTR-MS is considered as soft, meaning little or no fragmentation of the analyte ion. The product and primary ions are mass selected by a quadrupole mass analyzer and detected as ion counts by an electron multiplier. By knowing the magnitude of the ion-polar molecule collision rate for a given analyte, it should in theory be possible to obtain its concentration directly without the need of external calibration. The gas phase concentration of the trace analyte *R* in the aspired air is calculated by use of the collision rate and instrument parameters such as temperature, pressure and quadrupole transmission efficiency. Thus, PTR-MS has a potential for stationary real-time measurement of ICA in occupational air, as illustrated in a recent study where PTR-MS was used for quantitative measurements of ICA in air.[22] However, there is still a need for further evaluation and better characterization of the suitability of PTR-MS for ICA measurements in occupational air.

The aim of this study was to evaluate and document the applicability of PTR-MS for determination of ICA in workroom air, including establishment of the theoretical capture rate coefficient for ICA by quantum mechanical calculations. It was also a goal to investigate the influence of air humidity on the PTR-MS response for ICA, and to establish a correction factor for air humidity to improve the applicability of field measurements. Furthermore, it was sought to compare the PTR-MS response of quantitative ICA atmospheres to both indirect air sampling methods and well characterized standard atmospheres by Fourier transform infrared spectroscopy (FT-IR) as reference methods.

## Experimental

### Chemicals and supplies

Type 1 water was provided by a Milli-Q ultrapure water purification system (Millipore, Bedford, MA, USA). Cyanuric acid (98 %), formic acid (≥ 98 %), toluene (≥ 99.7 %), ethyl isocyanate (EIC) (98 %), phenyl isocyanate (PhI) (99 %) and propyl isocyanate (PIC) (99 %) were purchased from Sigma Aldrich GmbH (Steinheim, Germany), while hexamethylene diisocyanate (HDI) (> 99 %) and urea (≥ 99.5 %) was purchased from Fluka Chemie GmbH (Buchs, Germany). Di-n-butylamine (DBA) (≥ 99 %), analytical grade methanol (MeOH), glacial acetic acid (100 %) and hydrochloric acid (HCl) (37 %) was purchased from Merck GmbH (Darmstadt, Germany). Sulfuric acid ($H_2SO_4$) (Scanpure) was purchased from ChemScan AS (Elverum, Norway). Di-n-butylamine-$d_9$ (DBA-$d_9$) was obtained from Ramidus AB (Lund, Sweden), while acetonitrile (ACN) (HPLC grade) and methanol (HPLC grade) were acquired from Rathburn Chemicals Ltd. (Walkerburn, Scotland). Synthetic air (99.999 %), argon (99.999 %) and nitrogen (99.999 %) were obtained from YaraPraxair (Oslo, Norway). The VOC calibration gas TO-14A Aromatics Mix containing a mixture of 14 VOCs blended in nitrogen gas was obtained from Restek (Bellefonte, PA, US).

### Dynamic generation of ICA in test chamber

Dynamic atmosphere generation of ICA was achieved by continuous thermal decomposition of an aqueous solution of urea to yield ICA and $NH_3$,[23] using a modified version of a previously reported instrumental set-up.[24] The dynamic atmosphere generator is depicted in fig. 1. In order to obtain a stable spray and ICA generation the $H_2O$ was evacuated to avoid formation of bubbles during the nebulization process. The urea solution was filtered (pore size 0.22 µm) prior to infusion. The urea solution was delivered at a flow rate of 3.0 µL $min^{-1}$ (Pump 11 syringe pump, Harvard Apparatus, Massachusetts, US). The urea solution was nebulized using a Model MCN-100 nebulizer (CETAC Technologies, Nebraska, US) with preheated nitrogen (200 °C) as nebulizer gas at a flow rate of 1.0 L $min^{-1}$. The spray was passed through a glass wool insulated glass tube made in-house with varying inner diameters. The first section of the glass tube (I.D. 9 mm) the tube was surrounded by a short cylindrical furnace set to 275 °C (l = 120 mm) (Model MHS 20, Perkin Elmer, Massachusetts, USA) in order to pre-dry the spray, prior to introduction to a wider bore section (I.D. 44 × 350 mm) placed inside a cylindrical furnace Model CTF 12/65/550 (Carbolite Ltd., Hope Valley, England) set to 450 °C, to thermally decompose urea. At the end of the glass tube the urea decomposition products were mixed with humidified synthetic air delivered at a rate of 14 L $min^{-1}$ and directed into the test chamber. The humidifier unit consisted of three heat regulated (22 °C) 500 mL gas washing bottles (Schott AG, Mainz, Germany) coupled in parallel containing $H_2O$. A gas line parallel to the humidifier allowed for regulation of the humidity.

Needle valves, a BIOS Drycal DC-Lite air flow calibrator (Mesa Laboratories, Inc., Colorado, US), a ChipCap-L combined temperature and humidity monitor (GE Sensing, Billerica, Massachusetts, US) and a Defender 510H flow meter (Mesa Laboratories, Inc.) were used for air flow, temperature and humidity regulation. The ChipCap-L sensor was coupled to a PicoLog data logger (Pico Technology, Cambridgeshire, UK). The internal calibration of the ChipCap-L sensor was inspected and if necessary adjusted against a HumidiProbe (Pico Technology) while fitted together in the same chamber.

The dynamically created ICA atmosphere was directed concentrically 120 cm into a 210 L electropolished stainless steel (SS) cylinder (I.D. 420 mm × 1.5 m), and was allowed to travel back through the length of the cylinder to achieve atmosphere homogeneity before exiting through two ventilated outlet ports on the end plate of the chamber. The chamber was flushed 10 times its volume with the generated atmosphere preceding air sampling. Air samples were collected through ¼” SS toggle valves (Valco Group AS, Sandnes, Norway), which were evenly distributed on the end of the chamber, allowing parallel sampling through 12 channels. The chamber temperature and humidity were monitored continuously and the chamber was evacuated between experiments using a vacuum pump (Sogevac SV65, Oerlikon Leybold Vacuum GmbH, Cologne, Germany).

### Quantum mechanical calculations of the theoretical capture rate coefficient for ICA

All geometries were pre-optimized at the semi-empirical parameterized method number 3 (PM3) theory level.[25, 26] Hybrid density functional theory (DFT) calculations using Becke’s three-parameter exchange functional[27] and the gradient-corrected functional of Lee, Yang and Paar[28] (B3LYP),[29] were performed to optimize geometries and compute dipole moments and polarizabilities. All calculations were done using the Gaussian 03 Revision B.03 program suite[30] (Gaussian, Inc., Wallingford, CT, USA). Dunning’s correlation-consistent basis set with diffuse function-augmented basis sets with triple zeta (aug-cc-pVTZ) was employed.[31, 32] The permanent dipole moment ($\mu_D$) and isotropic polarizability ($\alpha$) of ICA were used to compute the ICA specific *Su and Chesnavich* capture rate coefficient $k_{SC}$ for the ion-polar molecule reaction occurring in the PTR-MS drift tube at 60 °C (333 K).[33] The proton transfer reaction rate coefficient $k$ (*equation 1*) for ICA at the specific PTR-MS operating conditions $\approx k_{SC}$, due to the exothermic nature of the reaction.[16] The calculated $k$ value for ICA was $2.89 \times 10^{-9}$ $cm^3$ $s^{-1}$. Furthermore, $k$ values for other occurring air contaminants detected in this study were calculated similarly.

### PTR-MS measurements

A Compact PTR-MS (Ionicon Analytik GmbH, Innsbruck, Austria) was operated with $H_3O^+$ as reagent ion. Sulfinert® treated SS tubing with I.D. 1.0 mm (Restek, Bellefonte, PA, USA) was used as inlet line (l = 1.2 m). The inlet and water vapour flow was adjusted to 1.0 L $min^{-1}$ and 6.0 sccm $min^{-1}$, respectively. The inlet and ion source chamber temperature was set to 60 °C. The Pressure Controller (PC) was set to 318 mbar, while the drift voltage was set to 600 V. The voltages for source, source out, drift tube, extraction lens, and nose cone were set to 65, 100, 600, 150 and 6 V, respectively, while the ion source plasma current was set to 6.0 mA. Instrument transmission was accounted for prior to experiments using the VOC calibration gas TO-14A Aromatics Mix (Restek) consisting of a mixture of 14 VOCs blended in nitrogen gas. The concentration of the VOCs in the calibration gas was established by the supplier with an analytical accuracy of ± 10 %. Single ion monitoring (SIM) of the $[M+H]^+$ ions of ICA, MIC and ACN was performed for mass-to-charge (*m/z*) values 44, 58 and 59 Monitoring of the corresponding $[M+H]^+$ ions for MIC and ACN was done for supplemental purposes only. The dwell time was set to 1 s for all ions. During real-time SIM while welding painted metal sheets the $[M+H]^+$ ions of EIC, PIC, PhI and HDI were recorded at *m/z* 72, 86, 120 and 169, were also recorded. The dwell time during welding was set to 200 ms for all ions.

### Fourier transform-infrared spectroscopy measurements

Static atmosphere experiments were done in a 250 L electropolished SS smog chamber equipped with a White type multiple reflection mirror system with a 128 m optical path length for rotational-vibrationally resolved Fourier transform-infrared spectroscopy (FT-IR). All experiments were carried out in synthetic air at 298 ± 2 K and 1000 ± 10 hPa. The IR spectra were recorded with an IFS 66v FTIR instrument (4000-400 $cm^{-1}$) (Bruker Corp., Massachusetts, US) employing an MCT detector.

FT-IR spectroscopic calibration curve for ICA was produced using a 23.2 ± 0.1 cm path cell where FT-IR spectra were acquired in the pressure range from 1.34 to 19.90 (± 0.15 %) mbar at 9 pressure levels. At each pressure level, 6 × 32 scans were co-added at a nominal resolution of 1.0 $cm^{-1}$ and Fourier transformed using boxcar apodization. This calibration was used for FT-IR quantification of ICA measured in the region 2320 – 2200 cm$^{-1}$ throughout this study.

### PTR-MS vs. FT-IR response

For establishment of the PTR-MS response for ICA, atmospheres containing ICA were created in the FT-IR smog chamber with absolute humidity (AH) between 1.2 to 16.3 ± 0.1 g m$^{-3}$ (6 to 72 ± 2 % relative humidity [RH] at 25 ± 2 °C), covering the ICA concentration range from 26.7 to 490.2 ppb. At each concentration level, FTIR spectra were recorded. 3 × 128 scans were co-added at a nominal resolution of 0.125 cm$^{-1}$ and Fourier transformed using boxcar apodization. Subsequent sampling with PTR-MS was performed through a port in the smog chamber.

Pure ICA was made by thermal decomposition of cyanuric acid.[34] Approximately 200 mg cyanuric acid was placed in a glass tube and inserted into a Model 12/65/550 tube furnace. The cyanuric acid was initially heated *in vacuo* and held at 120 °C for 30 minutes to remove any traces of water. The glass tube was subsequently sealed from the vacuum followed by heating at 6 °C min$^{-1}$ to 400 °C, after which the contents were condensed in a cold trap cooled by liquid nitrogen. The frozen ICA (melting point: - 80 °C)[34] product was vacuum double distilled and transferred to a separate container for storage (- 22 °C) or direct use. When ICA was stored in a freezer (- 22 °C), polymerization of ICA occurred. However, ICA was still present in the gaseous state after 2 weeks.

ICA atmospheres were created by transferring a specific amount of synthesized ICA from a 500 mL flask into the evacuated smog chamber. Humidity was created by introduction of a gravimetrically measured amount of water by the aid of a heat gun and synthetic air. The smog chamber was then filled with synthetic air to a pressure approximately 5 % over ambient pressure. The atmosphere was allowed to homogenize for 15 minutes and the surplus pressure was released into a flexible 25 L Tedlar® sampling bag (DuPont, Wilmington, DE, USA). During PTR-MS sampling from the smog chamber, the bag allowed the atmospheric and smog chamber pressure to equalize. Thus, the reaction conditions in the PTR-MS were unaffected by any external pressure differentials. Lower atmospheric concentrations of ICA were created by evacuating the chamber to a certain pressure and then adding water and synthetic air. The release of air into the Tedlar® bag was done for all atmosphere dilutions. Every sequence of dilutions was finalized by PTR-MS aspiration of the VOC calibration gas. Protonated benzene (*m/z* 79) was used to correct for potential instrument drift since the last transmission adjustment. Temperature and humidity were continuously monitored during sampling using ChipCap-L.

### Indirect sampling methods and liquid chromatography-mass spectrometric measurements of derivatives

Parallel air sampling with personal samplers was performed from generated dynamic atmosphere through the 12 toggle valve ports of the test chamber.

*Denuder.* Air samples were collected on freshly prepared denuders impregnated with equimolar amounts of DBA and acetic acid in MeOH (*n* = 4). The denuders were prepared according to a previously reported method.[35] Glass fiber (GF) sheets measuring 203 × 254 mm (MG160) (Munktell Filter AB, Falun, Sweden) were cut to pieces measuring 25 × 60 mm and 13 × 60 mm which were impregnated with a total volume of 1 mL 1.5 M DBA:Acetic acid in MeOH. Circular GF (MG160) filter discs (ø = 13 mm) were impregnated with 100 µL 0.7 M DBA:Acetic acid in MeOH. The MeOH was allowed to evaporate for 1 hour. The larger GF piece (25 × 60 mm) was rolled around a glass rod and inserted into a 3 mL luer lok syringe (B&D, Franklin Lakes, NJ, USA). The smaller GF piece (13 × 60 mm) was folded lengthwise into a v-shape, and inserted into the same syringe. The circular GF filter was inserted into a Millex 13 mm filter holder, which was attached to the syringe. The sampler was capped before transportation. The sampling flow rate was set to 0.2 L min$^{-1}$ using Casella Tuff personal air sampling pumps (NY, USA) equipped with a low flow adapter (SKC, Eighty Four, PA, USA). After sampling, the filter material from the denuders was transferred to test tubes that were spiked with 50 µL 10 ng µL$^{-1}$ ICA-DBA-$d_9$ and 5 ng µL$^{-1}$ MIC, EIC, PIC, PhI and HDI-DBA-$d_9$ derivatives as internal standards. 3 mL of 1 mM $H_2SO_4$ (aq), 3 mL MeOH and 6 mL toluene was added to the tubes, followed by 20 minute agitation, 10 minute sonication, 10 minute agitation and 10 minute centrifugation at 2300 rpm (Rotofix 32, Andreas Hettich GmbH & Co.KG, Tuttlingen, Germany). The toluene phase was transferred to new tubes prior to addition of 6 mL toluene to the remaining polar fraction and repetition of the extraction procedure. The two toluene fractions were merged and evaporated to dryness under a stream of nitrogen. The residues were dissolved in 0.5 mL ACN and sonicated for 10 minutes. Finally, the solutions were filtered and transferred to 1.5 mL glass vials. The calibration standards spiked with 500 µL calibration solution (*n* = 8) were treated as the samples. The calibration solutions contained 0.08 – 3 ng µL$^{-1}$ ICA-DBA (in ACN) and 0.006 – 0.25 ng µL$^{-1}$ MIC, EIC, PIC, PhI and HDI-DBA (in ACN). For the reagent to be present at an equal amount as in the samples, 1.1 mL of the MeOH was replaced with 1.1 mL 1.4 M DBA in MeOH.

*Impinger + filter.* Impinger flasks with 15 mL anhydrous toluene containing 0.01 M DBA were backed up by a Millipore filter cassette (MG 160, 25 mm GF filter) (Munktell Filter AB, Falun, Sweden). Air samples (*n* = 4) were drawn through the impingers at a sampling flow rate of 0.5 L min$^{-1}$ using SKC Universal personal air sampling pumps. A Defender 510L primary flow calibrator (Mesa Laboratories, Inc.) was used for measurement and adjustment of all sampler flows. After sampling the impinger solutions and corresponding filters were transferred to test tubes. 50 µL internal standard solution was added to all tubes. The tubes were sonicated for 10 minutes and the solutions were transferred quantitatively to new tubes. The toluene was evaporated to dryness under a stream of nitrogen. The residues were dissolved in 0.5 mL ACN and sonicated for 10 minutes. The solutions were filtered and transferred to 1.5 mL glass vials. Calibration standards (*n* = 8) were prepared by spiking impinger solutions (15 mL toluene containing 0.01 M DBA) with 500 µL calibration solutions. The calibration solutions contained 0.01 – 1 ng µL$^{-1}$ ICA-DBA and MIC-DBA (both in ACN).

A method described elsewhere[36] for preparation of 1-(2-methoxyphenyl)piperazine derivates of ICA, was modified for preparation of DBA and DBA-d$_9$ derivatives of ICA. Urea (3.9 g), DBA/DBA-d$_9$ (0.814 g) and 125 mL $H_2O$ was refluxed for 3 hours at 125 °C using a thermostated oil bath. The solution was then transferred to a separating funnel and acidified with 4 drops of HCl (37 %). The resulting ICA-DBA/DBA-d$_9$ derivatives were extracted with 4 × 10 mL toluene, prior to evaporation to dryness under a stream of nitrogen. Isocyanate/diisocyanate-DBA and DBA-d$_9$ derivatives of MIC, EIC, PIC, PhI and HDI were synthesized according to a method described elsewhere.[35] Stock solutions of the derivatives were prepared by dissolution in acetonitrile.

A liquid chromatography-mass spectrometry (LC-MS) system consisting of a CapLC™ capillary gradient pump and a Micromass QuattroLC tandem quadrupole (MS/MS) (Waters, Massachusetts, USA) was used for separation and quantification of isocyanate-di-n-butylamine (DBA) derivatives. 1 µL sample solution in a partially filled 5 µL sample loop containing 4 µL $H_2O$/ACN 90/10 (%, v/v) focusing liquid was introduced onto a Kromasil® C$_{18}$ column (1.0 mm I.D. x 15 cm) (AkzoNobel, Separation Products, Bohus, Sweden) with 3.5 µm particles and pore size 100 Å, at a flow rate of 40 µL min$^{-1}$. The sample was eluted using a gradient from 30 % to 95 % B in 10 minutes followed by 8 minute hold at 95 % B. Reconditioning of the column was done with 30 % B for 5 minutes. Solvent A consisted of $H_2O$, and solvent B consisted of ACN. Both solvents contained 0.05 % formic acid. Detection of isocyanate-DBA derivatives was done in the positive electrospray mode. The capillary voltage was 3.8 kV, while the cone voltage was 25-30 V. The RF lens and extraction cone voltages were 0.3 V and 2 V, respectively, while the multiplicator voltage was 650 V. The source and desolvation gas temperature was 110 °C and 350 °C, respectively. The desolvation gas flow was 360 L h$^{-1}$. Multiple reaction monitoring (MRM) was performed to monitor up to 10 ions with a dwell time of 0.3 s. The collision energy was 15-16 eV. Argon was used as collision gas, and the collision cell pressure was set to 2.7 × 10$^{-3}$ mbar.

### PTR-MS measurement of thermal decomposition products during welding of steel plates covered with HDI paint

Steel plates (d = 1 mm) were coated with 5 layers of a HDI-based 2-component paint using a Asturo 9011 HVLP pneumatic spray gun (Walmec, Trieste, Italy). The paint was allowed to cure for 3 days at 40 °C. The painted steel plates were cut into 5 cm strips and approximately 5 mm of the edges were sanded clean to avoid contamination of the weld, as usually practiced prior to welding. Continuous PTR-MS monitoring was employed for *m/z* 28 (HCN), 44 (ICA), 58 (MIC), 59 (acetone), 72 (EIC), 86 (PIC), 100 (BIC), 120 (PhI), 169 (HDI) during the welding process using the respective calculated reaction rates *k*. The dwell time was set to 200 ms for all ions. Complementary personal (*n* = 3) and stationary (*n* = 3) denuder air sampling was performed at a sample air flow rate of 0.2 L min$^{-1}$. The denuder sampling time was 10 - 16 minutes.

## Results and discussion

### PTR-MS response versus FT-IR response of ICA

Preliminary experiments indicated a negative influence from humidity on the detection efficiency of ICA by PTR-MS. Since the air humidity may vary substantially with seasonal changes, and since the elevated temperatures in use for work operations where thermal decomposition might occur also can influence on the air humidity, it was necessary to examine the impact of air humidity on the PTR-MS detection efficiency of ICA. In a previous study where PTR-MS has been reported as a promising technique for ICA determinations from air[22] indirect sampling using impingers was used as quantitative reference for the "true" air concentrations of ICA. Unfortunately, indirect air sampling methods have limitations in this regard. At high RH, impingers suffer from condensation in the sampler mainly due to the cooling of the sampler solution caused by evaporation.[35] Such condensation may interfere with isocyanates in the sample air stream leading to lower sampling efficiency. Especially the sampling efficiency of ICA has been demonstrated to be strongly affected by high relative sample air humidity.[35] Such effects were observed during preliminary experiments in the present study as well (results not shown). Nevertheless, airborne isocyanates have been collected with good correlation between different samplers,[35] despite the non-optimal potential to act as quantitative reference method for generated standard atmospheres.

Another limitation regarding the characterization of dynamically generated ICA atmospheres, is the rather complicated generation process usually involving initial thermal degradation of a nebulized aqueous urea solution, as compared to generation of traditional VOC atmospheres where quantitative solutions of the components of interest usually are directly nebulized and evaporated, thus making available easy calculations of the true air concentrations.[37] Thus, when to further investigate the potential of using PTR-MS for determination of airborne ICA a direct and selective reference method is to be preferred over an indirect method.

FT-IR spectrometry is a well characterized technique providing direct sensitive and selective detection of ICA in the laboratory without spectral interferences. The long light path (128 m) in the corresponding smog chamber offers adequate detection limits. Therefore, FT-IR was chosen as a reference method for establishing the true value for the concentration of ICA in air. Since the FT-IR measurements, apart from PTR-MS and pumped indirect methods, do not consume air, the need for a dynamic ICA generation method is ruled out. Thus, an easier setup where ICA atmospheres are generated directly from ICA in gaseous state generated by thermally decomposed cyanuric acid is attractive. Unfortunately, for practical reasons this generation method is not easy applicable for dynamic generation of ICA atmospheres for PTR-MS and indirect methods, which usually involves the nebulization of solutions at a constant flow.
The FT-IR calibration of generated ICA yielded a linear response

($R^2$ = 0.995) in the pressure range 1.34 – 19.90 mbar, where the pressure is equivalent to an absolute amount of ICA molecules in the given volume covering the relevant concentration range in this study. Initial experiments when using dry atmospheres (AH 1.2 g m$^{-3}$) revealed that the PTR-MS response was approximately 25 % of the FT-IR response throughout the stated concentration range. The water content in the drift tube is in large excess of ICA. It is thus suspected that the loss of signal is mainly due to hydrolysis of ICA[34] in the drift tube:

$$HNCO + H_2O \rightleftharpoons NH_3 + CO_2 \qquad (3)$$

Any additional water introduced via the sample line is expected to further affect the equilibrium of *equation 3* to the right. The negative influence on the detection efficiency has also has been observed for formaldehyde[38, 39] and HCN[40] when using PTR-MS.

The stable relationship between the FT-IR and PTR-MS response for ICA, independent of concentration level within the investigated range relevant for typical occurring occupational air concentration levels, makes available the establishment of a PTR-MS correction factor (*f*). However, this relationship might be influenced by the air humidity during sampling. Thus, comparison of ICA measurements with PTR-MS and FT-IR was performed at an AH of 1.2, 9.9 and 16.3 ± 0.1 g m$^{-3}$ with ICA concentration ranges of 26.7 – 435, 72.7 – 490 and 44.8 – 358 ppb, respectively. The three humidity conditions resulted in variations in PTR-MS response on equivalent concentrations levels, while the FT-IR response was not influenced by humidity. A reduction of the PTR-MS signal for ICA of approximately 50 % was observed when humidity was increased from dry to humid (approximately 1 to 16 g m$^{-3}$), in accordance with the observations in another study.[22] Increased humidity in the sampled air resulted in an increased amount of the water cluster $H_3O^+{\cdot}H_2O$, measured at *m/z* 37. The ratio of the ion intensity between the water cluster $H_3O^+{\cdot}H_2O$ (*m/z* 37) and $H_3{}^{18}O^+$ (*m/z* 21), as a function of AH exhibited a second order polynomial relation (fig. 2). Thus, if not external temperature and humidity measurements are logged during sampling, AH can easily be obtained via the *m/z* 37/21 ratio recorded by the PTR-MS.

The influence of humidity on PTR-MS detection efficiency of ICA demonstrated, however, a linear behavior ($R^2 > 0.999$) (fig. 3), which makes a correction factor for PTR-MS ICA response available also correcting for humidity effects based on the FT-IR response. The corrected PTR-MS data for all investigated (pooled) concentration and humidity levels yielded a near uniform (slope = 0.974) and linear ($R^2$ = 0.993) relation to the FT-IR responses (fig. 4), while the uncorrected PTR-MS responses also exhibited linear responses throughout the concentrations ranges for the investigated AH levels of 1.2, 9.9, 16.3 g m$^{-3}$ ($R^2$ = 0.984, 0.956 and 0.989, respectively).

The "true" ICA air concentrations based on the actual PTR-MS measurements can thus be calculated by

$$PTR-MS_{corrected} = \frac{PTR-MS_{measured}}{f} \qquad (4)$$

where PTR-MS$_{corrected}$ is the "true" ICA air concentration, PTR-MS$_{measured}$ is the uncorrected measured ICA air concentration, and the correction factor *f* (the relative PTR-MS response in relation to the FT-IR reference response) = 0.2532 - 0.73 × AH (fig. 3). *Equation 5* expressed in the parametric form is given by

$$PTR\text{-}MS_{corrected} = \frac{PTR\text{-}MS_{measured}}{0.2532 - 0.73 \times AH} \qquad (5)$$

The analytical quantification of ICA using FT-IR in the smog chamber was done with an analytical uncertainty of better than ± 10 %.[41] The limit of detection (LOD) for ICA using FT-IR was 20 ppb, based on a signal-to-noise ratio (S/N) of 3. The LOD for PTR-MS was defined as S/N of 2 times the standard deviation of the background signal.[42] The instrumental LOD for ICA was 2.3 ppb, based on S/N = 2. Unfiltered humid atmospheres resulted in slightly higher LODs for ICA of 3.4 and 7.8 ppb, at an AH of 4.0 and 15.5 g m$^{-3}$, respectively. All LODs presented are obtained by response correction using *equation 5*.

The establishment of the LODs was based on extrapolation below the FT-IR calibration range (due to the LOD for FT-IR). Nevertheless, the presented PTR-MS LODs are close to the LODs acquired in another recent study.[22] A lower LOD can be obtained by increasing dwell time at the cost of time resolution. When monitoring air in conjunction with thermal decomposition, it may be necessary to apply a short dwell time to properly detect transient peak concentration values.

The PTR-MS within-day instrument drift of the mean signal of ICA was 3.2 % (4.5 % RSD, *n* = 8) in the concentration range 3.4 - 638.5 ppb.

### Verification of PTR-MS calibration with indirect sampling methods

The applicability of the PTR-MS calibration method obtained in this study was examined by off-site measurements of ICA in dynamic standard atmospheres generated by thermal decomposition of urea from an aqueous solution. ICA was generated with an efficiency of approximately 80 %, based on PTR-MS corrected measurements using *equation 5*. Stable atmosphere generation (6 % RSD, *n* = 1400) was attained after 2.5 hours, as measured with PTR-MS at approximately 600 ppb. From the point of steady-state, a stable atmosphere could be provided for about 6 hours as the gas supply was a single flask of synthetic air.

Air sampling was performed using parallel sampling with impinger (*n* = 4) and denuder samplers (*n* = 4), with a sampling time of 10 to 30 min, simultaneous with continuous monitoring of *m/z* 44 with PTR-MS. An atmosphere was generated containing ICA at a concentration of approximately 640 ppb (5.0 % RSD) after correction with an AH of 15.6 ± 0.1 g m$^{-3}$ (82 ± 2 % RH, 22 ± 0.6 °C). The relative recoveries of the LC-MS measurements of the ICA-DBA derivative related to the corresponding corrected PTR-MS response where 99.9 (9.3 % RSD) and 79.6 (8.1 % RSD) % for the impinger and denuder sampling, respectively. This adds further to the applicability of using portable PTR-MS for stationary measurements of thermally decomposed ICA in occupational hygiene, making available real-time direct measurements, short sampling times, identification of peak exposure events and avoidance of subsequent time- and labor demanding laboratory analyses.

### Thermal decomposition of cured HDI-paint

Plasma welding of HDI-painted sheets of steel was done while performing continuous PTR-MS sampling drawing air approximately 80 cm above the welding spot. The appearing concentration corrected trace for *m/z* 44 is presented in fig. 5. The AH used in the correction was derived from the ion intensity ratio of *m/z* 37/21. Several peak values were detected, illustrating the benefits of a direct-reading instrument over time-averaged measurements. The concentration spikes had a typical base width of 5 to 10 seconds. The sharpness of the spikes indicates the possibility of peak clipping. Although the dwell time was 200 ms, eight other ions were monitored for supplemental purposes. Consequently, each data point represent one measurement cycle which is 3.25 s in length.

During thermal decomposition of polyurethanes, other isocyanates are also formed[2, 4, 43] and may act as interferences while monitoring ICA using PTR-MS. The signal of m/z 44 is the principal ion for ICA, as well as for EIC (44 (100), 72 (12)).[22] Thus, *m/z* 44 accounts for 89 % of the EIC response for PTR-MS. For the purpose of confirmation and identification of any potential interference, complementary stationary and personal air sampling was done using denuders. The stationary samples were collected close to the sampling inlet of the PTR-MS. Dry methods, such as denuders, are usually preferred over impingers for personal sampling in relation to hot work like welding due to reduced fire hazard.[44] Sequential denuder samples confirmed the presence of ICA with total mean values of 34.4 ppb (75.4 % RSD, $n$ = 3) and 98.5 ppb (28.7 % RSD, $n$ = 3) for the stationary and personal samples, respectively, illustrating the variability in ICA generation during the welding process. EIC was also detected with total mean values 0.2 ppb (97.7 % RSD, $n$ = 3) and 0.7 ppb (47.4 % RSD, $n$ = 3) for the stationary and personal samples, respectively. The fraction EIC/(ICA+EIC) (ppb) is 0.6 and 0.7 % for the stationary and personal denuders, respectively. Since [ICA]>>[EIC], the contribution of EIC is negligible. The mean concentration of ICA in the same time-frame as denuder air sampling measured with PTR-MS was 42.6 ppb (170 % RSD, $n = 815$, AH was 10.2 g $m^{-3}$). The high variability reflects the variable emission of fumes. The relation $ICA_{denuder, stationary}/ICA_{PTR-MS}$ (ppb) is 80.6 %, which coincides well with the relative recovery obtained from the controlled laboratory experiments using dynamically generated ICA atmospheres (79.6 %).

The entire welding procedure lasted for about 45 minutes over three welding sessions in a small non-ventilated room. The spikes observed at approximately 50 minutes (fig. 5) resulted in primary ion intensity reduction to roughly 70 % due to the amount of decomposition products consuming the primary ion. If the decrease in $H_3O^+$ is larger than 10 %, the quantification using a particular ion $(M+H)^+$ is compromised due to loss by secondary chemistry in the drift tube,[45] resulting in underestimation of analyte concentration. When using PTR-MS for long term measurements it is important to be aware of this restriction.

## Conclusions

A method is presented for calibration of a compact PTR-MS instrument which enables direct, concentration and humidity independent real-time quantification of ICA. Interferences must be considered when measuring complex atmospheres using PTR-MS. Application of complementary air sampling techniques is still advisable for the purpose of confirmation of thermal decomposition products. The PTR-MS technique offers low maintenance and reproducible measurements over time.

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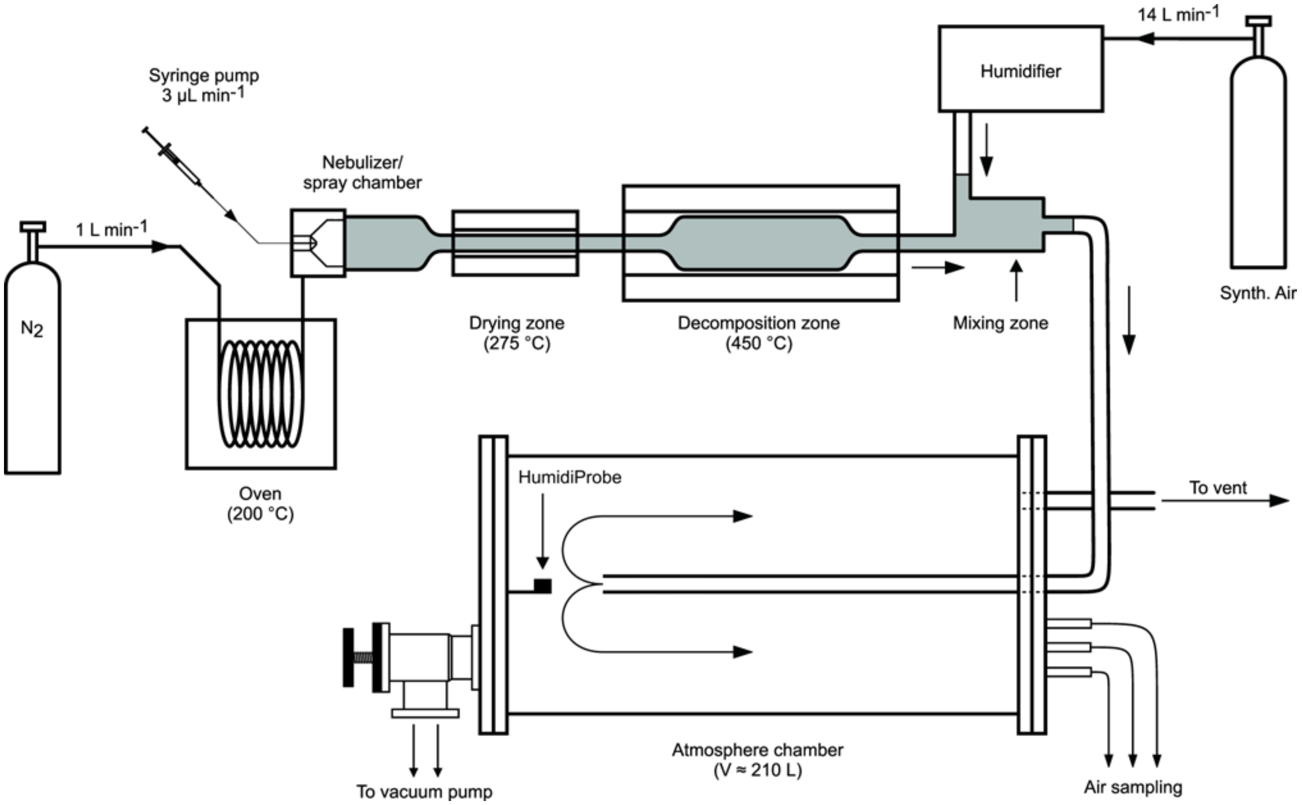

**Fig.1** A schematic representation of the dynamic atmosphere generation setup. The glass tube with varying diameters is highlighted with gray color.

5

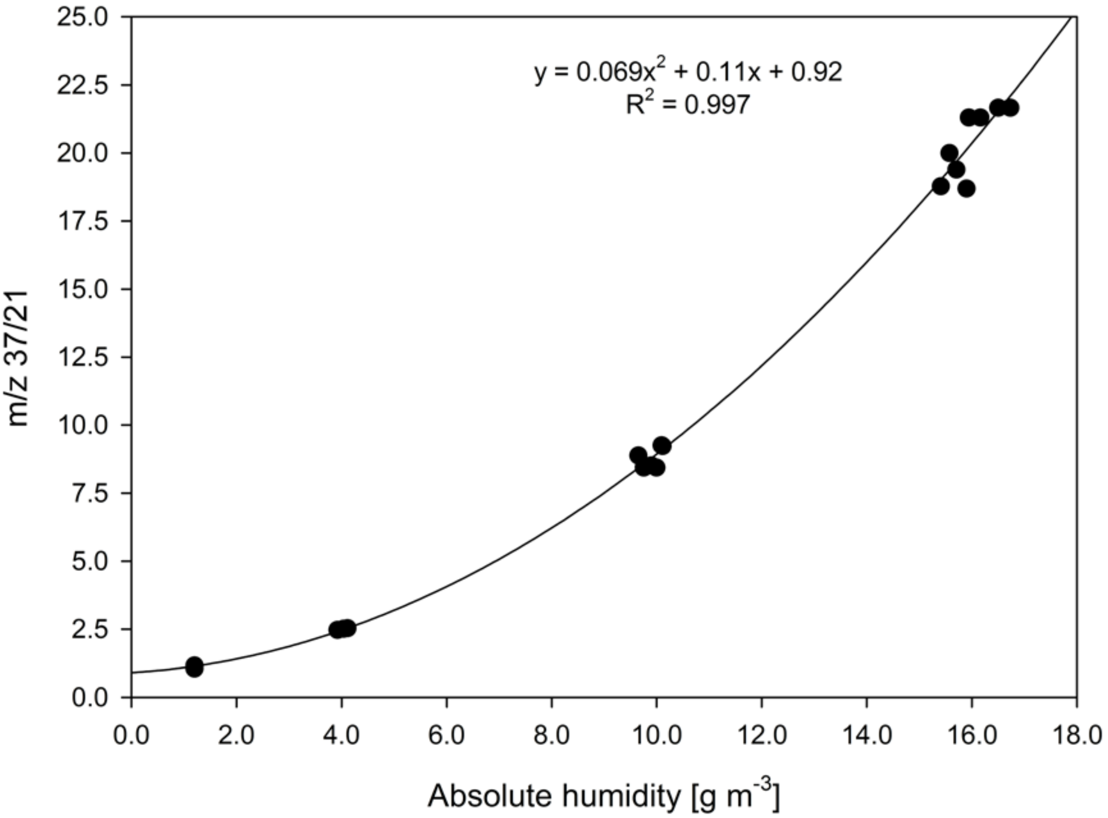

**Fig.2** The ratio of the ion intensity for m/z 37/21 as a function of sample air absolute humidity. The lowest data point correspond to synthetic air. The line is a second order regression fit. Each point is represented by *n* = 30 measurements.

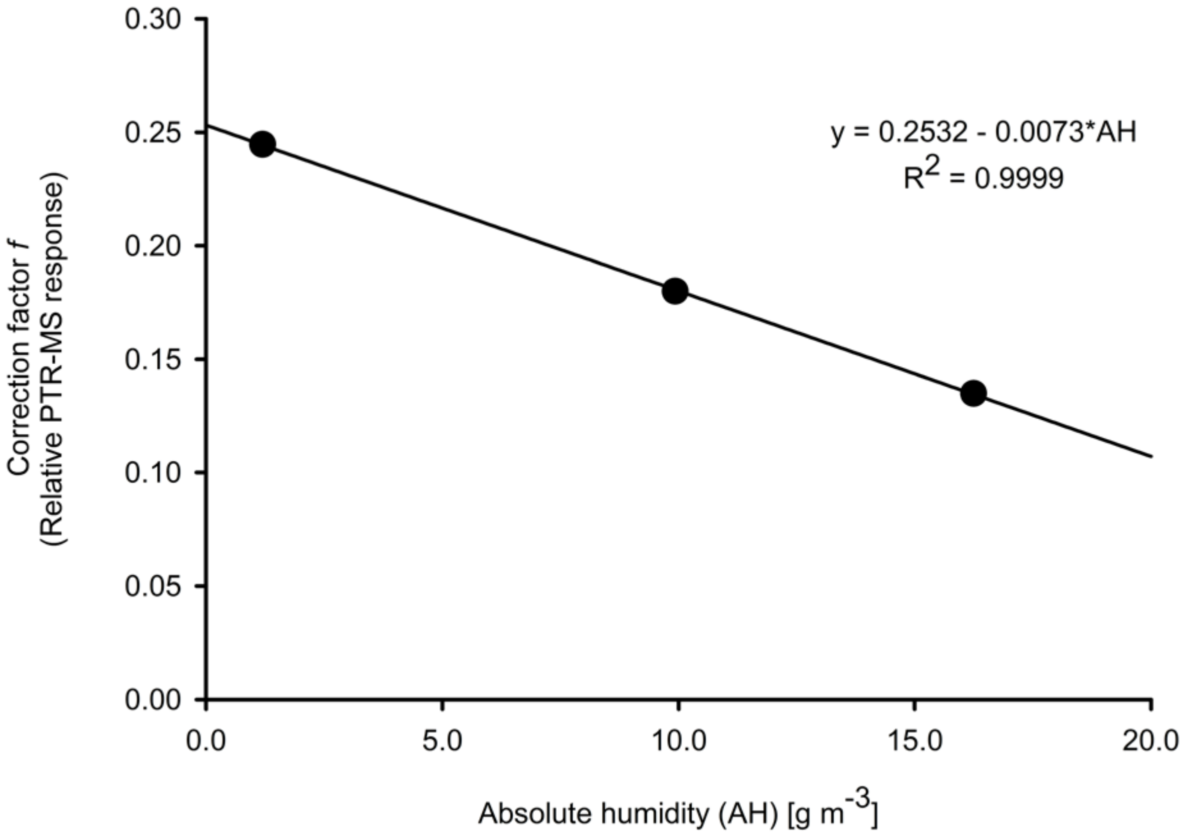

**Fig.3** PTR-MS response efficiency of HNCO as a function of absolute humidity (AH) in sample air. The AH (± 0.1 g m$^{-3}$) is derived from temperature and relative humidity measurements. The line is a linear regression fit.

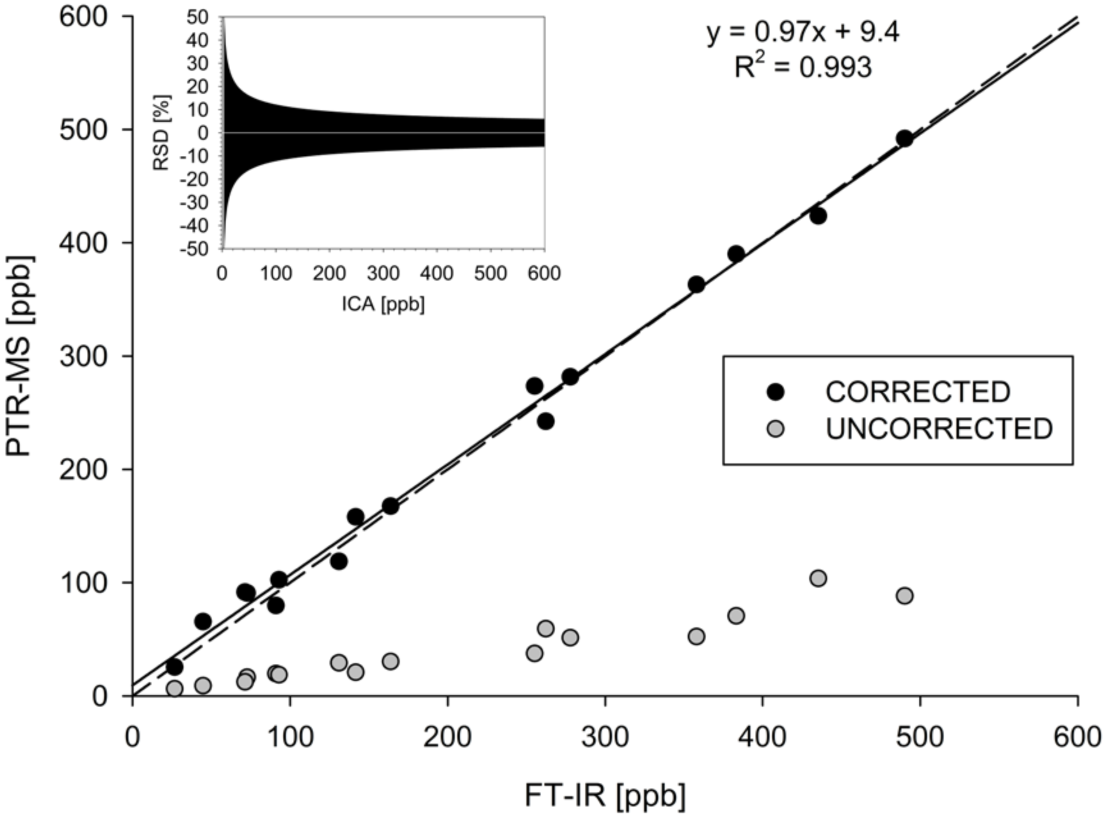

**Fig.4** Scatterplot of HNCO obtained by FT-IR and PTR-MS. The dotted line show the x = y line. PTR-MS data measured at *m/z* 44 in HNCO atmospheres (uncorrected) with absolute humidity (AH) 1.2 to 16.3 ± 0.1 g m$^{-3}$ (6 to 72 % relative humidity at 25 ± 2 °C), was adjusted with respect to AH (corrected). The solid line is a linear regression fit to the corrected data. The insert describes the variation of PTR-MS noise (RSD) as a function of ICA concentration (ppb). 5

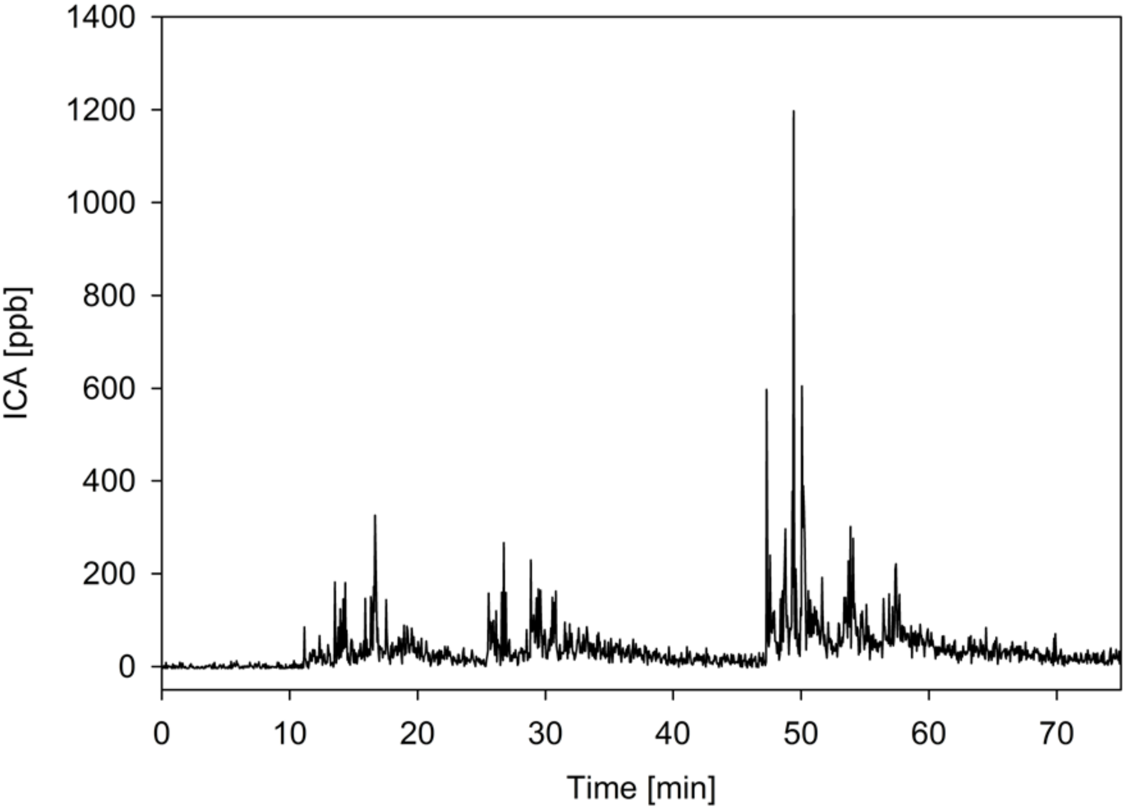

**Fig.5** PTR-MS recording of mass-to-charge ratio *m/z* 44 during plasma welding of steel sheets coated with HDI-paint. The trace data is corrected with respect to response efficiency.