



Sampling of Respirable Isocyanate Particles

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ABSTRACT

An advanced design of a denuder impactor (DI) sampler has been developed for characterization of possible airborne isocyanate exposure in different particle size fractions. The sampler is equipped with 12 different parallel denuder tubes, 4 impaction stages with the cut-off values (d_{50}) of: 9.5, 4, 2.5 and 1 μm , and an end filter that collects particles < 1 μm . All collecting parts were impregnated with di-n-butylamine DBA as the reagent in a mixture with acetic acid. The performance of the DI sampler was studied on a standard atmosphere containing gas and particulate isocyanates. The isocyanate atmosphere was generated by liquid permeation of 2,4-, 2,6-Toluene Diisocyanate (TDI), 1,6-Hexamethylene Diisocyanate (HDI) and Isophorone Diisocyanate (IPDI). 4,4'-Methylene Diphenyl Diisocyanate (MDI) particles were generated by heating of technical MDI and condensing the mixture of gas and particle-borne MDI in an atmosphere containing mixed salt particles. The study was performed in a 0.85 m³ environmental chamber with stainless steel walls. With the advancement of the DI sampler it is now possible to collect isocyanate particle samples for up to 320 min. The performance of the DI sampler is essentially unaffected by the humidity. The DI sampler and the ASSET™ EZ4-NCO sampler (Sigma-Aldrich/Supelco, Bellefonte, PA, USA) gave similar results. Sample losses within the DI sampler are low. In the environmental chamber it was observed that the particle distribution may be affected by the humidity and ageing. A scanning mobility particle sizer (SMPS) was used to separate a flow of selected fractions containing MDI particles from mixed MDI and salt particles. The particle-size distribution had a maximum at about 300 nm, but later in the environmental chamber 1 μm dominated. The distribution was very different as compared to with only NaCl or MDI present. The biological relevance for studying isocyanate nano particles is significant as these have the possibility to reach the lower airways where allergic reactions may occur. SMPS and isocyanate air sampling can be used for the investigation of isocyanate nano particles.

KEYWORDS: aerosol; air sampling; DBA; denuder; impactor; isocyanate; respirable

INTRODUCTION

Occupational exposure to isocyanates within the polyurethane (PUR) industry is known to cause irritation and chronic airway disorders such as asthma (Baur

et al., 1994; Ott *et al.*, 2003). Exposure may occur during thermal degradation of PUR or other nitrogen containing polymers (Karlsson *et al.*, 1998, 2001) and during production of PUR (Rando *et al.*, 1987;

Tinnerberg *et al.*, 1997). The presence of isocyanates in the workplace atmosphere occurs in both gas phase and/or associated with particles during work operations with PUR-materials (Streicher *et al.*, 2000). Particle-borne and/or gas-phase isocyanates can be formed at workplaces, e.g. while spray painting and during thermal degradation, such as grinding, torch cutting or welding of a PUR coated surface (Myer *et al.*, 1993; Karlsson *et al.*, 2000, Marand *et al.*, 2004; Woskie *et al.*, 2004).

Definitions of the size fractions for inhalable, thoracic and respirable particles were established by the International Organization for Standardization (ISO), the European Committee for Standardization (CEN) and the American Conference of Industrial Hygienists (ACGIH). Particles with an aerodynamic diameter size of $>10\ \mu\text{m}$ are deposited by inertial impaction in the upper air ways. The respirable particle fraction (entering the deepest part of the lungs) consists of the particles with an aerodynamic diameter size of $4\ \mu\text{m}$ at d_{50} (CEN/TR 15230:2005; Hinds, 1999).

The gas-phase diffusion efficiency for a cylindrical denuder has earlier been described by Zulfiqur *et al.* (1989). The gas-phase diffusion efficiency for the DBA denuder has been evaluated earlier both theoretically and experimentally by the authors (Gylestam *et al.*, 2013). The diffusion efficiency is dependent on a stable sample flow rate, the viscosity of the air, the diffusion coefficient and that the temperature is uniformly distributed in the denuder. As long as laminar flow can be achieved, the particle penetration has been shown to be unaffected by the diameter of cylindrical tubes for a given volumetric flow, which is opposite to the diffusion efficiency for analytes in gas-phase (Zulfiqur *et al.*, 1989; Hinds, 1999). The theoretical particle deposition by diffusion for a tubular denuder has been described earlier (Zulfiqur *et al.*, 1989; Hinds, 1999).

Due to the reactivity of isocyanates, the derivatization upon collection is necessary to minimise losses. It is most common to use secondary amines as derivatization reagents. Today, samplers are most often impinger flasks containing the reagents dissolved in an organic solvent or sampling filters coated with a reagent. For most current dry samplers field extraction is necessary to minimise sample losses.

A dual-filter system (ISO Check) using a PTFE filter for collection of particles in series with an impregnated glass fibre filter to collect the gas phase

isocyanates has been in use for the last two decades (Lesage *et al.*, 1992; ISO 17736:2010). A triple-filter system, with two PTFE filters in series with an impregnated glass fibre filter, has also been proposed (Tsai *et al.*, 2003). The use of non-impregnated PTFE filters can result in losses due to isocyanate side reactions, with other airborne compounds, prior to derivatization (Streicher *et al.*, 2000). For collection of MDI aerosols and HDI and HDI biuret a dichotomous sampler was proposed, using an annular impregnated diffusional denuder and filter in series (Rando and Poovey, 1994, 1999). Several other prototypes of size-selective isocyanate aerosol air samplers have been proposed (Koch *et al.*, 1997; Tatum *et al.*, 2002; Huynh and Vu Duc, 2008).

The impinger flask containing di-*n*-butylamine (DBA) solution with a filter in series has been shown to provide a separation of gas and particle phase ($0.1\text{--}1.5\ \mu\text{m}$) (Spanne *et al.*, 1999).

Sampling of isocyanates in the gas phase using a DBA-coated denuder with an end-filter in series has been proposed (Nordqvist *et al.*, 2001). Marand *et al.* (2005) proposed a dry sampler with a filter-coated cylindrical denuder with an end-filter in series. The filters were coated with DBA mixed with an equimolar amount of acetic acid to reduce the evaporation of DBA. The dry sampler was later refined by adding a V-filter in the tubular denuder and a double extraction step in the work-up to increase the sampling time, robustness and precision of the dry sample (Gylestam *et al.*, 2013, ISO 17734-1:2006). The dry sampler is commercially available (ASSET™ EZ4-NCO, Sigma-Aldrich/Supelco, Bellefonte, PA, USA) and have been used as a reference sampler in this study.

A DBA-impregnated denuder-impactor (DI) for gas and particle borne isocyanates that size-separated both gas and particle-borne isocyanates was presented by Dahlin *et al.* (2008). The isocyanates were collected using a DBA impregnated rectangular parallel plate denuder connected to a cascade impactor (DI) with DBA-acetic acid impregnated impactor plates.

The aim of this study is to advance the denuder cascade impactor technology for respirable airborne isocyanate particles and to study the performance of the sampler in an environmental chamber containing gas and particle-borne isocyanates.

EXPERIMENTAL

Chemicals

DBA, HDI, Isophorone Diisocyanate (IPDI) and Toluene Diisocyanate (80% 2,4-TDI, 20% 2,6-TDI) were obtained from Sigma-Aldrich (St. Louis, USA). Acetonitrile, acetic acid, formic acid, methanol and toluene were obtained from Merck (Darmstadt, Germany). 4,4'-methylene diphenyl diisocyanate was obtained from Agros Organics (NJ, USA).

The DBA derivatives and the DBA- d_9 derivatives of 1,6-hexamethylene diisocyanate (HDI), isophorone diisocyanate (IPDI), 2,4- and 2,6-toluene diisocyanate (TDI) have been synthesised in our laboratory (Karlsson *et al.* 2005). For 4,4'-MDI both DBA- d_9 and DBA- d_{18} derivatives were used. Deuterium-labelled DBA $[\text{NH}(\text{C}_4\text{H}_9)(\text{C}_4\text{D}_9)]$ obtained from Synthelec (Lund, Sweden) and $[\text{NH}(\text{C}_4\text{D}_9)_2]$ from C/D/N Isotopes Inc., Quebec, Canada were used for synthesis of internal standards. All solvents used were HPLC-graded or higher.

Instrumentation

LC-MS/MS

The isocyanates were analysed as their corresponding urea-derivatives using LC-MS/MS. The LC-MS/MS system consisted of a micro-LC pump (Shimadzu LC10ADVP, Shimadzu Inc., Kyoto Japan) with a CTC-pal autosampler (CTC Analytics AG, Zwingen, Switzerland) connected to a Quattro Micro (Waters, Altrincham, Cheshire, UK) mass spectrometer. The mass spectrometer was operated in the positive electrospray ionization mode performing multiple reaction monitoring (MRM) of $[\text{M}+\text{H}]^+ \Rightarrow [\text{DBA}+\text{H}]^+$. A 2.5 μl -sample was injected into a 20- μl sample loop containing 17.5 μl of a focus liquid of 5/95 (% v/v) acetonitrile/water solution. The flow rate was 70 $\mu\text{l min}^{-1}$ using an Xterra[®] C18, 50 mm $\times$ 1.0 mm with 2.5- μm particles (Waters, Massachusetts, USA). A gradient was used with the mobile phase of (A) 5/95/0.05 and (B) 95/5/0.05 acetonitrile/water/formic acid (v/v/v). Elution was performed using a linear gradient from 60% A to 100% B in 12 min. The gradient was followed by isocratic elution with 100% B during 3 min. The mass spectrometer was operating with capillary voltage of 4 kV, ion source was 130°C, and the desolvation gas temperature was 200°C. The desolvation gas flow was set to 500 l h^{-1} . Argon was used as collision

gas with a collision cell pressure of 3×10^{-3} mbar. Collision energies and entrance cone voltage were individually optimized for the different urea derivatives. Further description of the analysis for the urea derivatives are presented in Karlsson *et al.* (2005).

PTR-MS

A compact Proton Transfer Reaction Mass Spectrometry (PTR-MS) (Ionicon Analytik, Innsbruck, Austria) was used for isocyanate monitoring. The PTR-MS was operated with a source current of 7 mA, and the detector (channeltron) was set to 2100 volts. The drift tube pressure was 2.2 mbar and the pressure in the detection chamber was 5.2×10^{-5} bar. The water vapour flow was set to 6 ml min^{-1} , the inlet and ion source temperature was 70°C. The source and source-out voltages were 150 and 115 V, respectively. The drift tube, extraction lens and nose cone voltages were 600, 158 and 6 V, respectively. The isocyanates TDI, HDI and IPDI were monitored simultaneously with a dwell time of 5 s and with a pause time of 1 s and an inlet flow of 0.5 l min^{-1} . For TDI, the protonated molecular ion ($m/z = 175$) was monitored. For HDI and IPDI the fragment ions $m/z = 126$ and $m/z = 180$ amu were monitored, respectively (Gylestam *et al.*, 2011).

SMPS

A TSI Scanning Mobility Particle Sizer Spectrometer (SMPS) (TSI Inc., USA), TSI model 3080 electrostatic classifier, TSI model 3081 differential mobility analyser (DMA) and TSI model 3775 Condensation Particle Counter (CPC) operated in low-flow mode was used for particle monitoring (0.01–0.7 μm) during the DI particle tests. The SMPS was operated in continuous scanning mode with sampling resolution of 4 min, 2 min of up ramping of the voltage and 1 min of down ramping and 1 min of time out. Scanning was performed in the particle-size range of 14–700 nm with a sheath flow of 3 l min^{-1} and a sample flow rate of 300 ml min^{-1} . The classifier was equipped with a negative high voltage controller.

APS

A TSI Aerodynamic Particle Sizer Spectrometer (APS) 3321 system was simultaneously used with the SMPS system for particle monitoring during the DI particle tests. The APS was operated in continuous scanning mode in the particle size range of 0.56–20 μm with a

sheath flow of 4 l min^{-1} and a sample flow rate of 1 l min^{-1} and with a sampling resolution of 20 s.

Air sampling

For the DI tests air sampling was performed utilizing novel air sampling pumps (Pump prototype, IFKAN, Hässleholm, Sweden) at flow rate set to 2 l min^{-1} and to 200 ml min^{-1} for the reference method. Seven to eight different pumps were simultaneously used for the experiments in the DI tests. The flow-rate of the pumps was designed to be 2 l min^{-1} and $200 \text{ ml min}^{-1} \pm 2\%$. A TSI 4140 flow meter was used to confirm the sampling flow through the setup.

Environmental test chamber

An exposure chamber with a total volume of 0.85 m^3 was designed. The chamber consisted of stainless steel with manipulative gloves. Inside the chamber an LPKB 125 B mixing fan unit was mounted with flow rate range of $0\text{--}90 \text{ l s}^{-1}$ (Östberg Group AB, Avesta, Sweden). The chamber was connected to the exhaust ventilation propelled by an EKB HB 4520-220T high-power fan (EKB-produkter AB, Mölletofta, Sweden). The air pressure was kept slightly lower in the chamber as compared to the ambient pressure. A conditioning system was used for controlling the temperature and humidity of the influent air. The studies were performed at 20°C with relative humidity in the range of 20, 50 and 90%. A Bürkert 8626 mass flow controller with an air flow of 500 l min^{-1} was used to regulate the influent air (Bürkert, Ingelfingen, Germany). The relative humidity was monitored with a Testo 645 (Testo GmbH & Co, Lenzkirch, Germany).

Condensation nuclei

Salt particles were generated from a $\text{NaCl}/\text{H}_2\text{O}$ solution with a pressurised air-driven nebulizer. The salt aerosol was dried and diluted in a 0.85 m^3 separate particle drying chamber with an influent flow of 200 l min^{-1} of dry pressurised air. The particle-drying chamber had an air pressure kept slightly over the ambient air pressure and was connected to the glass MDI mixing chamber. The particle-drying chamber consisted of stainless steel. Inside the chamber an LPKB 125 B mixing fan unit was mounted with flow rate range of $0\text{--}90 \text{ l s}^{-1}$. The outlet was connected to the exhaust ventilation. The air pressure inside the particle drying

chamber delivered about a 1 l min^{-1} salt aerosol flow into the MDI mixing chamber.

Isocyanate generation

Gas phase

An isocyanate atmosphere was generated by liquid membrane permeation of 2,4- and 2,6-toluene diisocyanate (TDI), 1,6-hexamethylene diisocyanate (HDI) and isophorone diisocyanate (IPDI). Permeation tubes of silicon rubber (length 11.5 cm ; OD 8 mm , thickness 2 mm , VWR International AB, Stockholm, Sweden) with varied volumes of isocyanates were placed inside a permeation chamber with a volume of 0.77 l . The temperature of the permeation chamber was controlled by placing the permeation chamber in a temperature controlled water bath ($35\text{--}40^\circ\text{C}$). To the permeation chamber an inlet flow of nitrogen was introduced at a flow rate of $2.5\text{--}5 \text{ l min}^{-1}$. The flow rate was regulated by using a constant flow regulator Brooks PC 8902 series and SHO-RATE GT1355 flow controller (Brooks automation, Inc., Chelmsford, MA, USA). The generated concentrations were controlled by varying the flow rate through the permeation chamber and varying the temperature of the permeation chamber. The generated gas-phase isocyanates were further diluted in the environmental chamber to constant concentrations, during the tests, in the range of $1\text{--}10 \text{ ppb}$.

Particle-borne isocyanates

The MDI aerosol was generated through heterogeneous nucleation of MDI vapour using dried salt particles as condensation nuclei. MDI particles were generated by heating technical MDI and condensing the mixture of gas and particle-borne MDI in an atmosphere containing mixed salt particles (Fig. 1). Preheated nitrogen regulated by a mass flow controller was introduced into a heated stainless steel generation chamber. The nitrogen flow (50 ml min^{-1}) was directed into/over a glass tube containing technical MDI. The generation flow was diluted with a preheated nitrogen flow (1.0 l min^{-1}). The diluted MDI vapour was then transported through a heated tube furnace and into a mixing chamber with a total volume of 0.03 m^3 . The mixing chamber was made of glass walls together with polypropylene walls. The mixing chamber had several internal glass walls to obtain better mixing. To the mixing chamber a flow of dried salt particles was

introduced. The generated MDI aerosol concentrations (about $3000 \mu\text{g m}^{-3}$) were controlled by varying the temperature ($150\text{--}190^\circ\text{C}$), generation flow rate and/or the salt aerosol flow rate.

The MDI aerosol containing both MDI/NaCl-particles and MDI vapour were introduced (about 2 l min^{-1}) to the environmental chamber using two copper tubing ($1/4''$ OD, $3/16''$ ID, length 0.5 m) as transfer lines. The aerosol was further diluted in the environmental chamber to appropriate concentrations in the range of $5\text{--}11 \text{ ppb}$ of MDI. Primarily MDI/NaCl-particles will be transported through the transfer lines. The MDI vapour will, due to low vapour pressure, adsorb to the surface in the transfer lines before entering the environmental chamber.

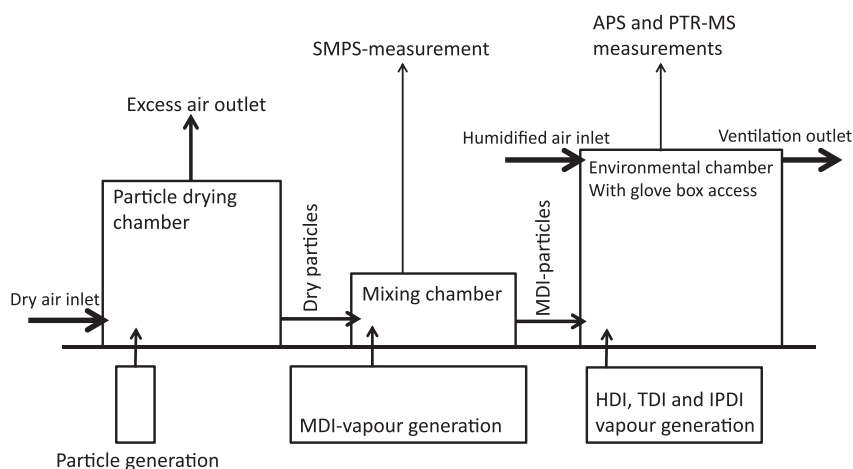
DI sampler

The DI sampler consisted of a pre-impactor stage, a denuder, a three-stage cascade impactor and an end

filter. The denuder part collects gas phase isocyanates. The particle-borne isocyanates are size fractionated in three steps in the cascade impactor, and particles $< 1 \mu\text{m}$ are collected on the end filter. The denuder consists of 12 different parallel denuder tubes. Four impaction stages were used in the DI with the theoretical cut-off values (d_{50}): $10, 4, 2.5$ and $1 \mu\text{m}$. The $10\text{-}\mu\text{m}$ impactor stage is a pre-impactor stage positioned before the denuder. The design parameters for all impactor stages are displayed in Table 1, and the design is presented in Fig. 2.

Reference method

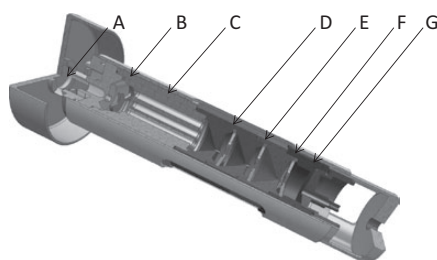
The ASSET™ EZ4-NCO sampler was used as reference sampler. The sampler was obtained from Sigma Aldrich/Supelco (Bellefonte, PA, USA). Work-up procedure and the analytical method has been previously described (Gylestam *et al.*, 2013, ISO 17734-1:2006).



1 Schematic picture of the isocyanate gas phase and particle generation system.

Table 1. Design parameters for the impactor stages

Impactor	Stage 1	Stage 2	Stage 3	Stage 4
Nozzle width (mm)	4.93	2.70	1.99	1.11
Jet to plate distance (mm)	6.41	3.51	2.59	1.44
Throat length (mm)	6.16	4.50	4.00	3.50
Reynolds number	572	1045	1417	2542
Calculated d_{50} (μm)	10.0	4.0	2.5	1.0



2 Cross-cut view of the denuder impactor. A: Rain cover. B: Pre-impactor stage $d_{50} = 10 \mu\text{m}$. C: Denuder consisting of twelve symmetric cylindrical tubes coated with an impregnated tubular glass fibre filter (tube-filter, $23.7 \times 57 \text{ mm}$) and equipped with a concentrated V-shaped impregnated glass fibre filter (V-shaped filter, $13.7 \times 57 \text{ mm}$). D-F: Impactor stages with d_{50} D = $4 \mu\text{m}$, E = $2.5 \mu\text{m}$ and F = $1 \mu\text{m}$. G: End filter ($0.3 \mu\text{m}$ pore size), collecting particles $< 1 \mu\text{m}$.

Preparation

Denuder

The sampler consisted of 12 polypropylene tubes ($L = 67 \text{ mm}$, $ID = 0.8 \text{ cm}$). The inner wall of each tube was lined with an impregnated glass fibre filter (tube-filter, $23.7 \times 57 \text{ mm}$) and a glass fibre filter strip ($13.7 \times 57 \text{ mm}$), folded as a 'V' placed inside the tube to increase the collection efficiency by increasing the number of channels in the tube. The glass fibre filters were of type MG 160 (Munktell, Grycksbo, Sweden). The samplers were prepared by mounting the filters in the tube and filter holder prior to impregnation. The mounted samplers were then impregnated with 1.5 ml reagent solution for each denuder tube, containing equimolar amounts of DBA and acetic acid in methanol, and they were then dried in a nitrogen flow (about 24 l min^{-1}) for 2 h. The impregnated denuders were kept under nitrogen in plastic zip bags and were stored in a refrigerator prior to air sampling.

Cascade impactor

The impactor plates, 13 mm i.d. MG 160, were placed in the impactor plate holders and impregnated with 50 μl of a saturated solution of DBA and acetic acid. The solution was obtained by mixing 2 ml DBA, 673 μl of acetic acid and 50 μl of H_2O . To achieve and maintain low viscosity for the solution, the DBA-acetic acid solution was kept in a water bath (about 50°C) during the impregnation of the impactor plates (Dahlin *et al.*, 2008).

End filter

Impregnation was performed by adding 300 μl of 0.74 mol l^{-1} of DBA and acetic acid in methanol solution to the end filter (MG 160) with a pore size of $0.3 \mu\text{m}$ and a diameter of 47 mm.

Work-up procedures

Denuder

After sampling, the tubular and V-shaped filters were collected and extracted ($n = 12$) with 3 ml of $1 \times 10^{-3} \text{ mol l}^{-1} \text{ H}_2\text{SO}_4$ (aq), 3 ml of methanol, 5.5 ml of toluene and 100 μl of the internal standard solution (IS, 10 ng of each of the corresponding isocyanate DBA- d_9 -derivatives) in a double extraction procedure, as described previously (Gylestam *et al.*, 2013).

The denuder was rinsed with 12 ml toluene. The toluene was transferred to test tubes and 100 μl IS was added. The extracted toluene phase and the rinsing toluene (about 11 ml) and the excess DBA-reagent were removed by evaporation to dryness (model SC210A; Savant Instruments Inc., Holbrook, NY, USA), and the dry residues were dissolved in 0.5 ml acetonitrile. The test tubes were placed in an ultrasonic bath for 10 min and manually shaken, and the sample solution (100 μl) was transferred to vials for injection into the LC-MS/MS. Calibration standards ($n = 8$) were prepared in spiked solutions (0.5–70 ng of 1,6-HDI, 2,4-/2,6-TDI, IPDI, 4,4'-MDI as DBA derivatives) and 10 ng IS. The calibration standards were evaporated and dissolved in 0.5 ml acetonitrile and analysed with the same procedure as the urea-derivatives (Karlsson *et al.*, 2005)

Impactor stages and end filter

Impactor substrate (impregnated filter from impactor plate 4, 2.5 and $1 \mu\text{m}$) and the end filter. After air sampling was completed the impactor-substrate and end filter were transferred to test tubes containing 5 ml toluene. 10 ng IS and 1.5 ml $1 \times 10^{-3} \text{ mol l}^{-1} \text{ H}_2\text{SO}_4$ (aq) was added. The samples were extracted by sonication for 10 min, shaking for 10 min and centrifuged for 10 min at 3000 rpm. The toluene was separated and transferred to new test tubes. The extracted toluene phase and remaining DBA-reagent were removed by evaporation of the solvent containing the analyte and the calibration standards in a vacuum centrifuge (model SC210A; Savant Instruments Inc., Holbrook,

NY, USA), and the dry residues were dissolved in 0.5 ml acetonitrile (Dahlin *et al.*, 2008).

The test tubes with 0.5 ml acetonitrile and the isocyanate DBA derivatives were sonicated for 10 min and manually shaken, and a 100- μ l sample solutions were transferred to vials for injection into the LC-MS/MS. Calibration standards ($n = 8$) were prepared in spiked solutions (1–70 ng of 1,6-HDI, 2,4-/2,6-TDI, IPDI, 4,4'-MDI as DBA derivatives) and 10 ng IS. The calibration standards were evaporated and dissolved in 0.5 ml acetonitrile and analysed with the same procedure as the urea-derivatives (Karlsson *et al.*, 2005).

Particle collection efficiency of the impactor

The particle collection efficiency of the impactor was investigated. Particles were generated in a test chamber with a total volume of 0.5 m³. The chamber was made from wood and acrylic glass. The chamber was connected to the laboratory exhaust ventilation. In the test chamber a pressure slightly lower than the ambient pressure was maintained. Characterization of the particle collection efficiency of the impactor was done by connecting the different impactor stages to the inlet of a TSI APS 3321. Non-reactive spherical glass particles (Spherglass 5000 Solid Glass Spheres, Potter Industries Inc., USA) were dispersed using BEG 1000D and BEG 1000S (Palas, Germany) using compressed air. The sampling flow for the APS was 5 l min⁻¹, which was higher than the impactor sample flow of 2 l min⁻¹. Due to the different sample flow rates between APS and impactor a sheath flow (about 3 l min⁻¹ of compressed air) was presented to the APS using a T-connected sampling probe and a TSI 4140 flow meter. The impactor flow rate of 2 l min⁻¹ was regularly tested using a Gilibrator-2 air-flow meter (Sensidyne Inc., USA). The cut-off efficiency was investigated by measuring the number of penetrated particles with and without the different impactor stages present. The particle size with 50% cut-off marks the cut-off of d_{50} .

Particle collection efficiency for the end filter in the DI sampler

The collection efficiency for the entire sampler, that is, denuder, impactor stages and end filter, was investigated. The 0.85-m³ stainless steel chamber and MDI particle generation setup, described earlier, were used to achieve stable conditions. The setup consisted of a

DI sampler placed inside the chamber, connected to a sampling tube (copper, 1/4" OD, 3/16" ID, length 1 m). The sampling tube was drawn through the wall to the outside of the chamber and was connected to a stand-alone TSI CPC 3775, which measured the particle number concentration. The sampling flow of the CPC was 0.3 l min⁻¹, and the DI sampler demanded a sampling flow of 2 l min⁻¹; therefore, a split connection and an air sampling pump with a flow set to 1.7 l min⁻¹ was used to obtain a total air flow of 2 l min⁻¹ through the DI sampler. To eliminate any effects of losses in the sampling setup, the same setup was used to alternately sample the MDI-particle concentration inside the test chamber and the particle penetration through the DI sampler. A TSI 4140 flow meter was used to confirm the sampling flow through the setup. The filter collection efficiency for the DI sampler, at different particle-size fractions, was evaluated using a TSI SMPS system. The same sampling setup, as described earlier, was used during these measurements.

Sample losses in the DI

Gas phase

The losses of gas-phase isocyanates (HDI, IPDI and TDI) in the DI sampler, below the pre-selector and above the entrance to the denuder, were investigated. The gas-phase losses were tested using a PTR-MS system. The PTR-MS was connected to the DI through a 50-cm 1/16 inch PolyEtherEtherKetone (PEEK) tube. Two PEEK tubings equal in length and ID size were mounted at the inlet of the sampler and inside the sampler directly above the denuder entrance. The setup was then placed in the exposure chamber. The DI was exposed to gas-phase isocyanates (HDI, IPDI and TDI) in the concentration range of 10–20 ppb. During the measurements a sampling flow rate in the DI sampler was maintained at 2.0 l min⁻¹. The PTR-MS measured the background in ambient air. The PTR-MS was then connected, through a union, to the PEEK tube placed above the DI inlet and then switched for connection to the PEEK tube inside the DI. Each measurement was conducted for 15 min and repeated twice. The response inside the denuder cascade impactor and inside the exposure chamber was background-subtracted before calculation of the ratio of isocyanate gas-phase loss in the upper part of

the DI. All filters and impactor stages were analysed and all parts below the denuder were rinsed and then analysed.

Particles

The SMPS was used to separate selected fractions containing MDI particles. The SMPS separates particles according to their electrical mobility, which is proportional to the particle size. Before entering the DMA, where the size separation takes place, the particles are lead through a neutralizer, where the particles carrying a high charge can capture ions of opposite polarity. After a short period of time a well-defined bipolar charge equilibrium distribution is achieved (Boltzmann distribution) and only the positively charged particles are separated according to their size inside the DMA (when a negative high voltage controller is used). The different MDI particle fractions were then sampled using a denuder in series with a filter impregnated with DBA/acetic acid, similar to the DI sampler. The MDI collected in the denuder and the filter were analysed separately. The particles that were deposited in the denuder defined the particle losses. The ratio of MDI-deposited in the denuder to the MDI collected on the filter was calculated. The SMPS sheath flow was set to 1.6 l min^{-1} with a sample flow rate of 166 ml min^{-1} . An MDI particle atmosphere was generated and presented to the SMPS system using a sampling tube (copper, 1/4" OD, 3/16" ID, length 1 m). The flow rate in the SMPS system was maintained using pump prototype IFKAN (Hässelholm, Sweden) at flow rates set to 166 ml min^{-1} . Particle sizes between 102 and 914 nm were fractioned into nine different average particle sizes (102, 202, 300, 400, 496, 594, 711, 792 and 914 nm). Each fraction was sampled with triplicate ASSET™ EZ4-NCO samplers for 18 min. The background was monitored to obtain the average particle concentration during the test. The generated particle measurements were collected for 18 min in the beginning, in the middle and at the end of the tests of the background using the TSI SMPS system. The background was monitored by particle-size scans in the size range 15–710 nm with a sheath air flow rate of 3 l min^{-1} and a sample flow rate of 300 ml min^{-1} . Particle deposition in the denuder test required a total of 28 ASSET™ EZ4-NCO samplers, $n = 56$ (2 analyses, denuder and end filter, per sampler).

The gas-phase collection efficiency for the denuder
The gas-phase collection efficiency in the denuder was investigated. Three DI systems without the pre-selector were exposed to gas-phase HDI, IPDI and particle-phase MDI during 30 min sampling. The DI samplers were located in the middle of the exposure chamber. All filters and impactor stages were analysed, and all parts below the denuder were rinsed and then analysed.

Variation of sampling time

To be able to compare the results from the DI sampler and ASSET™ EZ4-NCO samplers, any sampling bias due to particle inertia and/or particle settling velocity must be determined. The flow conditions inside the environmental chamber were controlled to fulfil the Agarwal-Liu criterion sampling in still air (Agarwal and Liu, 1980). The bias when sampling from still or nearly still air arises due to two factors: (i) the particle settling velocity when the inlet flow is low and the sampler faces upwards or downwards, (ii) the inertia of a particle. Using the Davies criterion (Davies, 1968), the minimum probe size due to the inertial sampling criterion and the maximum probe size due to settling velocity, respectively, can be determined. The inlet diameter, inlet flow and particle relaxation time are used in these calculations. The bias due to particle settling velocity can be eliminated by placing the sampler horizontally.

Sampling, during five different sampling times (20–320 min) was performed in a standard atmosphere, at a relative humidity of 50% at 20°C, containing gaseous phase HDI, IPDI, TDI, MDI and particle phase MDI. The concentrations obtained from the DI and ASSET™ EZ4-NCO samplers operated simultaneously were compared. For each sampling time, three parallel DI samplers and three ASSET™ EZ4-NCO samplers were sampled simultaneously inside the environmental chamber. The five different sampling time tests required 15 DI samplers ($n = 240$), and 18 ASSET™ EZ4-NCO samplers.

RESULTS AND DISCUSSION

Particle collection efficiency of the impactor

The Dahlin *et al.* (2008) DI sampler has been advanced to achieve respirable particle fractionated sampling. The end filter diameter has been increased to decrease

the pressure drop and the flow velocity decreases over through the end filter by a factor of 10 as compared to the earlier DI sampler. The new impactor design regarding jet nozzle, throat length and the jet to plate distance was optimised to achieve a Reynolds number between 500–2000 which yields laminar flow (Marple and Liu, 1974; Marple and Willeke, 1976; Jurcik and Wang, 1995; Marple *et al.*, 2001). To achieve a sharp cut-off, the value of jet to plate distance divided by the nozzle diameter should be < 1 (Marple and Liu, 1974). A cut-off with the shape of a cumulative log-normal distribution can be characterised by the Geometric Standard Deviation (GSD). GSD (σ_g) is a unitless number, always ≥ 1.0 (Hinds, 1999).

The pre-impactor stage was designed to have a value of $10\ \mu\text{m}$ cut-off (d_{50}). In Fig. 3 it can be seen that the curve decreases below zero between 3 and $8\ \mu\text{m}$ with an increase of particle penetration when measuring the $10\text{-}\mu\text{m}$ cut-off. This is not a real result as the particle collection efficiency test with and without the impactor stage present gives a slightly different flow pattern, and the number of particles in this size range was limited. The cut-off was experimentally determined to be $9.5\ \mu\text{m}$, possibly due to poor statistical data for determination of the ‘true’ cut-off.

For the other stages the experimentally determined cut-off diameters were close to our design values, 4, 2.5 and $1\ \mu\text{m}$. The efficiency curve sharpness (σ_g) was calculated for the 10, 4, 2.5 and $1\ \mu\text{m}$ cut off stages to be 1.21, 1.31, 1.24 and 1.24, respectively, computed according to Hinds (1999). The pre-impactor

is present to eliminate particles $> 10\ \mu\text{m}$ before the denuder part of the impactor. The isocyanate particle studies described in this paper do not include the pre-impactor stage as it was revealed that gas-phase isocyanates were adsorbed in the pre-impactor stage.

Particle collection efficiency for the end filter in the DI sampler

The particle number collection efficiency was determined to be 99.9% for the end filter. The MDI/salt-particle load concentration was about 9000 particles cm^{-3} and the particle-size distribution showed a maximum at a particle diameter of about 200 nm. The particle-size distribution for the particles measured after the DI had a maximum at 15–30 nm.

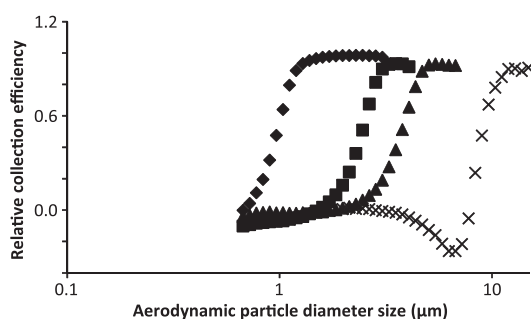
Sample losses in the DI

Gas-phase losses in the pre-impactor stage

The DI sampler was placed in a standard atmosphere, and isocyanates were monitored using a PTR-MS before and after the inlet (aluminium) and the pre-impactor stage (aluminium). The isocyanates present in the standard atmosphere were HDI ($90\ \mu\text{g m}^{-3}$), IPDI ($85\ \mu\text{g m}^{-3}$) and TDI ($120\ \mu\text{g m}^{-3}$) with a concentration RSD of about 5%. The isocyanates were then monitored before the entrance to the denuder part. Each measurement was conducted for 15 min and repeated twice. For the studied air concentrations, the tests demonstrated losses of about 10% for HDI and IPDI and 15% for TDI, of gas-phase isocyanate on surfaces of the pre-selector plate and entrance section. In field measurements, it is still recommended to use the inlet and the pre-impactor stage to avoid sampling large particles that are not respirable. Losses of gas phase isocyanates need, however, to be taken into account and may vary depending on isocyanate composition and the presence of other interfering compounds in the sampled aerosol. Isocyanate surface interactions have earlier been described as unavoidable due to isocyanates’ adsorptive properties (Holdren *et al.*, 1984).

Gas-phase losses after the denuder

The gas phase of HDI and IPDI losses as determined by washing the surfaces in the impactor were found to be $< 2.1\%$ with average in the range of 1.5–2.1% (RSD = 2.1–12.4%).



3 The collection efficiencies for the three impactor stages and the pre-impactor stage determined by measuring the penetration of spherical glass particles at a flow rate of $2\ \text{l min}^{-1}$. Impactor stage 1: $d_{50} = 1\ \mu\text{m}$ ($\blacklozenge$). Impactor stage 2: $d_{50} = 2.5\ \mu\text{m}$ ($\bullet$). Impactor stage 3: $d_{50} = 4\ \mu\text{m}$ ($\blacktriangle$). Pre-impactor stage 4: $d_{50} = 9.5\ \mu\text{m}$ ($\times$).

Particles losses

The MDI particle mass losses determined by washing the surfaces in the denuder were found to be < 1% with a RSD of 5.3%. A flow of MDI particles separated by the SMPS in 9 size fractions in the range of 101–914 nm were collected with the denuder in series with end filters. This demonstrated that sample losses of MDI particle mass in the impactor part excluding the pre selector are minor.

The MDI particle mass deposited in the denuder part was in the range of 1.6 – 3.7%. This demonstrates that even if we have not achieved an ideal laminar flow the particle deposition on the denuder walls is minor.

The gas phase collection efficiency for the denuder

The design has been altered, compared to the old DI sampler by Dahlin *et al.* (2008), to enhance the field and in-house handling by simplifying the assembly and work-up procedures.

The new denuder consists of a proven method with 12 tubular denuders with both tubular and a V-filter (Gylestam *et al.*, 2013). The sampling flow rate has been decreased to 2 l min⁻¹ and denuder filter area has also been increased by 17%, compared to the old DI sampler. By using the tubular DBA denuder system from the ASSET™ EZ4-NCO sampler (Gylestam *et al.*, 2013) it is possible to adopt the work-up in the routine analyses with small alteration of the work-up procedures compared to the ASSET™ EZ4-NCO sampler.

DI sampling was performed in a standard atmosphere containing isocyanates for 30 min at relative humidity of 50% and 20°C ($n = 3$). The standard atmosphere contained gas phase HDI (78.6 µg m⁻³), IPDI₁ (27.5 µg m⁻³) and IPDI₂ (12 µg m⁻³).

The denuder collection efficiency for HDI and IPDI was measured using three DIs. The average collection efficiency ranged between 95.1% and 96.5% (RSD = 0.2–0.8%).

The collection efficiency of HDI, IPDI and TDI in the tubular denuder filter was theoretically calculated according to Zulfiquar *et al.* (1989) and the efficiency of the V-filter was calculated according to Dasgupta *et al.* (1997) with the assumption that the flow fields in each channel are laminar and uniform. The theoretical collection efficiency was calculated to be in the range of > 98%. The experimentally observed gas phase breakthrough is similar to the calculated value.

Variation of sampling time

To be able to compare the results from the DI sampler and the ASSET™ EZ4-NCO sampler, any sampling bias due to particle inertia and/or particle settling velocity was determined. Since the inlet diameters for both samplers were already set, the maximum particle aerodynamic diameter, leading to no sampling bias, was calculated. For the DI sampler, at a sampling flow of 2 l min⁻¹ and inlet diameter of 47 mm, the maximum particle size that could be sampled without bias was >100 µm due to inertia and 5 µm due to particle settling velocity. For the ASSET™ EZ4-NCO sampler at a sampling flow of 200 ml min⁻¹ and inlet diameter of 8.2 mm, the maximum particle size that could be sampled without bias was 26 µm due to inertia and 9 µm due to particle settling velocity. Since the MDI particles generated during the tests in this study had an aerodynamic particle diameter < 2–3 µm, no sampling bias occurred according to the Davies criterion (1968).

Sampling was performed during five different sampling times (20 – 320 min), in the environmental chamber at a relative humidity of 50%. The predominately isocyanate gas-phase air concentrations were in the range of 14–29 µg m⁻³ for HDI, 80–105 µg m⁻³ for IPDI₁, 33–41 µg m⁻³ for IPDI₂ and 9–11 µg m⁻³ for 2,4-TDI. The 2,6-TDI concentration was about 2 µg m⁻³. MDI was present predominately in the particle phase in the range of 45–72 µg m⁻³. The amounts collected in the denuder cascade impactor were compared to those in the ASSET™ EZ4-NCO samplers sampled in parallel. For each sampling time three parallel DI samples and three ASSET™ EZ4-NCO samples were collected simultaneously inside the environmental chamber. The tests were performed over 3 days. Before and after each of the different sampling time tests the environmental chamber was opened, and samplers were changed. Because of experimental difficulties during this procedure it was not possible to revert to exactly the same concentrations. This is the reason why we cannot see a linear relationship between collected amounts of isocyanates with sampling time.

With a few exceptions the ASSET™ EZ4-NCO sampler and the DI sampler in total collected the same amounts of isocyanates (see Table 2). The DI sampler can collect isocyanates for up to 320 min. The ratio of the DI samples to the ASSET™ EZ4-NCO samples varied in the range of 0.63–1.20.

Table 2. Comparison of DI samplers ($n = 3$) and ASSET™ EZ4-NCO isocyanate air samplers ($n = 3$) at for sampling of standard atmosphere of gas phase isocyanate in the exposure chamber at four different sampling times (20–320 min) at RH 50%

		Sampling time (min)									
		20		40		80		160		320	
		Mg m ⁻³ ; RSD	Ratio	µg m ⁻³ ; RSD	Ratio	µg m ⁻³ ; RSD	Ratio	µg m ⁻³ ; RSD	Ratio	µg m ⁻³ ; RSD	Ratio
		(%)		(%)		(%)		(%)		(%)	
1,6-HDI	DI	20.9;	0.73 ^a	25.2;	0.94	19.2;	0.98	20.7;	1.14	15.1;	1.07
	sampler	6.4		12.9		11.9		26.4		6.7	
	ASSET Sampler	28.5; 10.3		26.7; 3.0		19.5; 4.4		18.1; 5.1		14.1; 4.9	
IPDI ₁	DI	81.1;	0.96	71.1;	0.89 ^a	90.2;	0.90	63.4;	0.63 ^a	90.4;	0.86
	sampler	8.3		1.8		11.1		12.1		4.7	
	ASSET Sampler	84.9; 9.3		79.6; 3.8		100.0; 3.4		101.9; 15		104.8; 9.2	
IPDI ₂	DI	29.6;	0.80 ^a	27.4;	0.82 ^a	38.9;	1.15	27.9;	0.69	37.3;	0.92
	sampler	8.8		7.9		11.7		13.8		7.1	
	ASSET Sampler	37.2; 6.6		33.3; 2.0		33.9; 4.9		40.2; 23.3		40.6; 19.9	
2,4-TDI	DI	7.1;	0.76 ^a	9.0;	0.80	9.9;	1.05	9.0;	1.20	8.0;	0.94
	sampler	7.1		17.6		16.3		19.5		11.0	
	ASSET Sampler	9.3; 4.3		11.2; 7.0		8.5; 5.3		10.7; 41.1		8.5; 12.8	
2,6-TDI	DI	1.9;	0.96	2.1;	0.93	2.0;	1.12	2.2;	1.20	1.7;	1.00
	sampler	9.4		15.1		20.1		32.2		8.8	
	ASSET sampler	2.0; 26.8		2.3; 20.3		1.8; 3.8		1.9; 15.5		1.7; 14.4	
4,4'-MDI	DI	74.7;	1.04	68.1;	0.96	56.2;	0.99	47.7;	1.06	46.1;	0.99
	sampler	4.9		3.7		20.0		11.2		0.6	
	ASSET sampler	71.8; 2.8		71.2; 8.3		57.0; 21.0		45.0; 2.3		46.7; 16.9	

^aSignificant differences between the isocyanate air samplers and the DI samplers at the 95% level using Student's *t*-test.

There were a few occasions of significant differences between the ASSET™ EZ4-NCO samplers and the DI samplers at the 95% level using Student's *t*-test, but there is no trend that can explain that this is due to chemistry or sampling efficiency that is related to the sampling time.

MDI particle size distribution in NaCl nucleus aerosol

When introducing NaCl particles into the mixing chamber a typical particle-size distribution was found. This distribution was about the same for a relative humidity in the range of 20–90%. Introducing only

MDI into the mixing chamber, the particle size number concentration was very low. When introducing MDI to an aerosol of NaCl particles the particle-size distribution changed dramatically as compared to only NaCl or MDI present (Fig. 4).

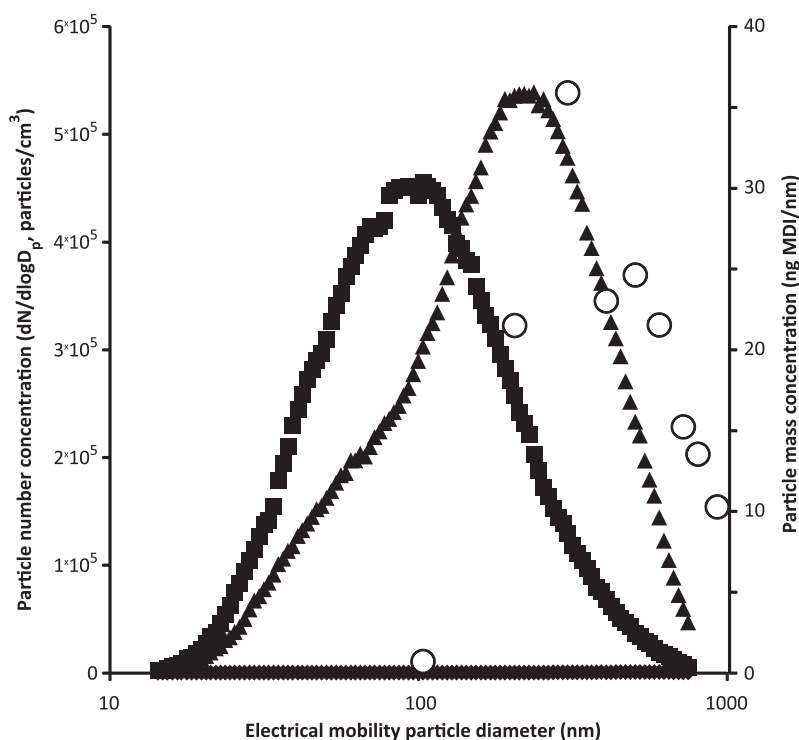
Nine different particle size fractions were collected using SMPS and a denuder in series with a filter impregnated with DBA/acetic acid, similar to the DI sampler. Three samples were collected for each particle fraction (see Table 3).

Since the size width of each channel (particle size fraction) increased with increasing particle size, the measured amount of MDI had to be normalized using the width of each channel. When sampling nine different fractions with the ASSET™ EZ4-NCO sampler and plotting the mass per nm (sampled amount divided by the channel width), it was observed that the mass particle size distribution had a maximum at about 300 nm. The maximum for the mass particle size distribution was shifted towards larger particle sizes compared to the number particle size distribution, which is consistent

with the theory. Compared to the mixing chamber the MDI number particle size distribution was very different in the environmental chamber tests, most likely due to ageing of the aerosol (see Fig. 5). The ageing of the MDI aerosol will be discussed in a forthcoming paper.

Influence of humidity for sampling of particle-borne MDI

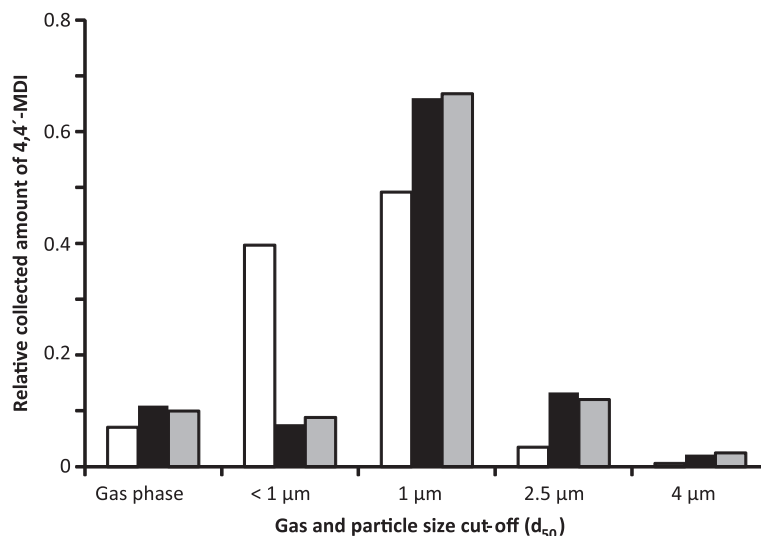
DI sampling in a standard atmosphere containing gas-phase and particle-phase MDI (in the environmental chamber) was performed over 2 days for 30-min sampling periods over a range of relative humidity (20–90%) at constant temperature (20°C). For each relative humidity tested, three parallel denuder cascade impactor samplers were operated simultaneously inside the environmental chamber. The three relative-humidity tests generated 9 denuder cascade impactor samples [$n = 144$ analytical samples; 9 denuder cascade impactors $\times$ (12 denuder filter analysis + 3 impactor stage filter analyses + 1 end filter analyse per denuder cascade impactor)], see Fig. 5.



4 Particle size distribution of: MDI associated to NaCl nuclei (▲), with an apex of 233 nm; only NaCl particles (•), with an apex of 101 nm; only MDI (◆); MDI concentration per nm (○, particle diameter, secondary Y-axis). RH was < 20%.

Table 3. Nine different particle-size fractions were collected using SMPS and a denuder in series with a filter impregnated with DBA/acetic acid, similar to the DI sampler. Three samples were collected for each particle fraction. RH was < 20%

Mid-point particle-size diameter (nm)	Span (nm)	MDI ($\mu\text{g sample}^{-1}$)	MDI (ng nm^{-1})	MDI RSD (%)
101.9	3.7	0.00	0.5	9.1
201.8	7.3	0.15	20.2	10.1
299.7	10.8	0.38	34.0	15.3
399.6	14.4	0.32	21.5	1.3
495.9	17.8	0.47	25.9	20.5
593.6	21.4	0.45	20.5	5.7
710.6	25.6	0.37	14.2	9.8
791.6	28.4	0.36	12.6	11.3
914.2	32.9	0.31	9.4	4.7



5 Gas and particle distribution of MDI at different relative humidity ($\square$ = 20% RH, $\blacksquare$ = 50% RH and $\blacksquare$ = 90% RH) and 20°C. The standard atmosphere contained $65.5 \mu\text{g m}^{-3}$ (RSD = 4.4%) MDI at 20% RH, $124.4 \mu\text{g m}^{-3}$ (RSD = 1.3%) MDI at 50% RH, and $124.1 \mu\text{g m}^{-3}$ (RSD = 6.4%) MDI at 90% RH.

In Fig. 5 it can be seen that the gas and particle distribution is affected by the humidity. At low humidity the small particles <1–1 μm dominate. For a relative humidity of 50% and 90% the particle sizes 1–4 μm dominate. The mechanism and chemistry for this is not yet understood, and future studies are necessary.

CONCLUSIONS

With the advancement of the DI sampler it is now possible to collect isocyanate particles in the particle size range of < 1, 1, 2.5 and 4 μm for 320 min. The performance of the DI sampler is essentially unaffected by the humidity, but the generated particle size

distribution varies slightly with humidity. The results for DI sampler and the ASSET™ EZ4-NCO sampler are very similar. Sample losses within the DI sampler are low, but the denuder parts must be rinsed and included in the analysis. In the environmental chamber it was observed that the particle distribution may be affected by the humidity and ageing. SMPS and ASSET™ EZ4-NCO sampler sampling can be used for the investigation of isocyanate nanoparticles.

The biological relevance for studying isocyanate nanoparticles is significant as these have the potential for reaching the lower airways where allergic reactions may occur (D'Alessio *et al.*, 1999; Wichmann *et al.*, 2000).

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