ASD# 101

First paper using CIP-10 for "chemical harvesting" of aerosols, This one for MDI isocyanate
This a first example to use this concept

Analytical Methods

PAPER

Adaptation of CIP10 for the sampling of 4,4′-methylene diphenyl diisocyanate aerosols

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Some sampling comparison studies have demonstrated that impinger and filter methods are not adequate for personal sampling of MDI aerosols in fast polymerization reaction processes. Other available sampling techniques for isocyanates have not been characterized for this application. These limitations led to the development of a new sampling method for MDI aerosols. The sampling method recommends a CIP10 device with a configuration in which a centrifuged liquid medium composed of DMPS + MOPIP (0.5 mg mL^{-1}) would collect the MDI aerosols. The DMPS + MOPIP medium was characterized in the laboratory and the MDI–MOPIP monomer and oligomer derivatives were quantitatively extracted using 4 extractions with acetonitrile. Moreover, the DMPS does not prevent the fast reaction between the free MDI and MOPIP, and reaction rates similar to those in an impinger were obtained for the free MDI monomer and oligomers in the DMPS + MOPIP medium. The LOD and LOQ of the method were 0.010 μg mL^{-1} and 0.033 μg mL^{-1} respectively. The dynamic range was from 0.079 μg mL^{-1} to 0.787 μg mL^{-1} with $R^2 \geq 0.990$. The intra-day and inter-day precisions were <6% for all of the concentration levels tested, and the accuracy was within an appropriate range of 100 ± 6%. No matrix effect was observed, and a total recovery of 98% was obtained. The method under the current conditions optimized in the laboratory appears suitable to be tested in the workplace for MDI aerosol sampling and to be compared in a real situation with an impinger.

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Introduction

4,4′-Methylene diphenyl diisocyanate (MDI) monomer and oligomers are used in the application of spray polyurethane foam insulation. During application, the workers can be overexposed to these substances. It is well documented that the MDI monomer and oligomers are strong sensitizers and respiratory and cutaneous irritants. The main consequence of work-related overexposure to MDI is occupational asthma.[1–6] The high toxicity of this substance requires an Occupational Exposure Limit (OEL) of 5 ppb for the MDI monomer in air[7–11] adopted by most countries. It has also been shown that workers can be affected by levels of isocyanates well below the OEL.[6,12–14] The toxicity of the total isocyanate functional groups must be considered, since oligomers induce asthma as much as the monomers.[15] From this perspective, the MDI monomer and oligomers in air must be appropriately evaluated in order to efficiently protect the workers using these chemicals.

The concentration of MDI in air associated with the application of polyurethane spray foam has been documented for residential construction.[16] Many conclusions have been drawn from this study. One of the conclusions was related to the comparison of filters and impingers for collecting the samples. Sampling methods involving filters have systematically underestimated the levels of MDI compared to the methods using an impinger. From this study and also from accepted facts about isocyanate air sampling practices using filters,[17,18] it is obvious that alternative sampling methods are needed to appropriately evaluate fast polymerization reaction processes involving MDI. The field use of an impinger is not practical due to the solvent contained in the sampling device. The risk of explosion associated with volatile and flammable solvents, the fragility of the impinger flasks, and a reduced sampling time have led to unfavorable conditions for personal sampling. However, filter sampling methods are solvent-free, eliminating most of the outcomes of the impinger sampling methods, but the underestimation of real MDI concentrations prevents their widespread usage for MDI sampling in the case of fast polymerization reaction processes as in polyurethane foam spraying. Improved MDI sampling approaches compared to impinger and filter methods are needed.

For some time, the cylindrical denuder has been introduced in the literature as a sampling device for isocyanates,[18,19] including MDI. A commercial version of this sampling device is also available and is known as the ASSET technology.[20] With this sampling technique, personal sampling can be efficiently done because no solvent and no field extraction are needed, and it is

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reported that the results obtained are comparable to the results that an impinger would have provided. However, the evaluation and validation of the ASSET sampler for use with MDI oligomers are still needed and the commercialization of derivatized MDI oligomers for this method is expected and would be useful. The evaluation with fast-curing MDI aerosols is also needed. Moreover, the recommendation with this sampling device is to use a low sampling rate of 200 mL min^{-1}. It is believed that such a low sampling flow rate would be efficient only in a limited number of applications, and a wider characterization of the device, in particular for MDI aerosol sampling in fast polymerization reaction processes, would be needed. Other sampling devices have also been used for isocyanate sampling, but so far their applications are limited to hexamethylene diisocyanate (HDI).[21,22]

Additional samplers are commercially available, but to date, they have not been used for specific sampling in fast polymerization reaction processes with MDI. This is the case with the device called CIP10.[23] CIP10 is a sampling device collecting air samples at a high sampling flow rate. The device was initially designed to collect dust, and changing configurations allows the collection of the alveolar, inhalable or thoracic fractions. Other CIP10 configurations are also available for collecting microorganisms in a centrifuged liquid medium.[24] The device can operate independently for up to 40 hours and is suitable for personal sampling. As this sampling device operates at high sampling flow rate, it is believed that its usage for MDI aerosols could provide an alternative and efficient way to sample MDI in fast polymerization reaction processes. The objective of this paper is to describe the adaptation of CIP10 for the sampling of MDI aerosols through the introduction of a non-volatile co-solvent with a derivatization agent in the device.

Experimental

Chemicals

MDI (98% purity), 1-(2-methoxyphenyl)piperazine (MOPIP; 98% purity), dimethylpolysiloxane (DMPS; viscosity 5 cSt), dimethylsulfoxide (DMSO; >99.9%) and acetic anhydride (AA; 98% purity) were obtained from Sigma-Aldrich (Milwaukee, USA) and were used without any further purification. Mondur 541 polymeric MDI (pMDI) was obtained from Bayer Material Science (Leverkusen, Germany). Acetonitrile (ACN), water (H_2O), both optima grade, and sodium acetate (99.4% purity) were obtained from Fisher Scientific (Canada). Glacial acetic acid was obtained from J.T. Baker. Toluene (99.9% purity) was obtained from EMD Millipore Corp. (Billerica, MA, USA). The in-house synthesis of the MDI–MOPIP monomer derivative and the purity check were done using a known and reliable procedure.[25] The in-house synthesis of MDI–MOPIP oligomers was done using the same protocol as for the MDI–MOPIP monomer, except that the MDI monomer was replaced by pMDI.

Instruments and analytical conditions

The HPLC-PDA system consisted of an Agilent series 1100 HPLC system (Mississauga, ON, Canada). The analytical column used was Luna C18, 3 μm, 3 mm × 150 mm from Phenomenex (Torrance, CA, USA). The software used to operate the system and analyze the data was Chemstation. The calibration curve regression was linear fit.

The mobile phase was composed of ACN (eluent A) and water + 92 mM sodium acetate adjusted to pH 6 with acetic acid (eluent B). The eluents were degassed with a 13 mm Acrodisc CR13 PTFE filter syringe, 0.2 μm from PALL Corporation Life Science (Ville St-Laurent, QC, Canada). HPLC separation was achieved using an isocratic program of 60% eluent A for 40 minutes. The flow rate was 0.6 mL min^{-1} and the column was kept at room temperature. The injection volume was 20 μL. The PDA detector was operated between 200 and 400 nm and the quantification was done at 250 nm.

Extraction of MDI–MOPIP from the DMPS

A solution consisting of 0.5 mg of MOPIP per mL of DMPS was prepared. 1 mL of this solution was transferred to test tubes. A known amount of the MDI–MOPIP derivative was spiked into the MOPIP–DMPS solutions. The concentrations of the spiked solutions were 0.3 μg mL^{-1}, 1.0 μg mL^{-1} and 2.0 μg mL^{-1}, which correspond to sampling for 15 minutes at 1 L min^{-1} at 15%, 50% and 100% of the OEL. After spiking, 1 mL ACN was added to the test tube. The test tube was vortexed for 20 seconds and the upper layer of ACN was transferred to another test tube. The extraction was repeated 4 times and the upper layers were combined in the same test tube. The ACN collected was then evaporated to dryness and dissolved in 1 mL of 20% DMSO/80% ACN + 0.5% AA. This solution was directly injected into the HPLC-PDA system. All attempts were done in 5 replicates each time. This procedure was used for the MDI–MOPIP monomer and the MDI–MOPIP oligomers.

Protocol to assess the reactivity of MDI in DMPS

To mimic the CIP10 conditions, 1 mL of 0.5 mg MOPIP per mL DMPS was divided into several test tubes. Then, 4 μL of a solution of 0.2 mg MDI per mL toluene was added to the MOPIP–DMPS solutions and vortexed. Following the addition of this solution, 1 mL of 0.5% AA in ACN was added at regular time points to stop the reaction between the MDI monomer and MOPIP upon reaction between AA and MOPIP. The time points were 1, 5, 10, 15, 30 and 60 min. The MDI–MOPIP derivative was then extracted using the protocol described in the previous section. To mimic the impinger conditions, 4 μL of 0.2 mg MDI per mL toluene was added to 1 mL of 0.1 mg MOPIP per mL toluene. The reaction was stopped as described previously. This solution was then evaporated to dryness and dissolved in 1 mL of 0.5% AA in ACN. The same protocol was repeated with the MDI oligomer except that 6 μL of 0.5 mg pMDI per mL toluene was spiked into the MOPIP–DMPS and MOPIP–toluene medium. The same time points and the same extraction protocol as for the MDI monomer assay were used. All attempts were done in duplicate each time.

Standard preparation

The MDI–MOPIP monomer and oligomer stock solutions were prepared separately by dissolving 20 mg of the respective

powder in 100 mL of DMSO. The calibration standards were prepared by spiking aliquots of the stock solutions in DMSO into the DMPS–MOPIP stock solution. Five calibration points were used for the MDI–MOPIP monomer. The concentrations of the calibration standards for the MDI–MOPIP monomer were 0.079 μg mL^{-1}, 0.118 μg mL^{-1}, 0.197 μg mL^{-1}, 0.394 μg mL^{-1} and 0.787 μg mL^{-1}. The MDI–MOPIP monomer and oligomer stock solutions were kept at 4 °C.

Analytical performance evaluation

The analytical parameters were evaluated for the MDI–MOPIP monomer using the extraction procedure described above. The recovery was investigated by comparing 6 replicates at 5 concentration levels spiked in DMPS + MOPIP (0.5 mg mL^{-1}) with replicates spiked into pure ACN. The concentrations of the replicates were identical to the ones used to build the calibration curve. The limit of detection (LOD) and the limit of quantification (LOQ) reported were based on a signal-to-noise ratio of 3 : 1 and 10 : 1 respectively. The intra-day precision was calculated from 6 separate measurements of 5 different concentrations in the desired dynamic range on a single day. The inter-day precision was calculated from 5 different concentrations distributed over the entire dynamic range and repeated 6 times for each measurement by the same person, on the same instrument, but on 6 different days. The accuracy was evaluated by analyzing a known concentration of MDI–MOPIP prepared from a second stock solution in the dynamic range and quantified using a standard curve.

Results and discussion

CIP10 strategy

The study evaluating the concentration of MDI in air associated with the application of polyurethane spray foam in residential construction[16] led to evidence that impinger and filter methods are not suitable for MDI sampling in fast polymerization reaction processes. From this study, it was determined that an alternative sampling method was needed. Considering that approaches involving a denuder or other available sampling techniques for isocyanates are also limited by different factors, the development of a new strategy for MDI sampling was necessary. The potential surrounding CIP10 promoted the idea of developing this sampling device for MDI. CIP10 allows sampling at a high rate of 10 L min^{-1}, which appears to be suitable for MDI aerosols. Also, the device is designed for personal sampling which is appropriate for evaluating the MDI concentration in the workplace at different workstations. Finally, the device can be adapted to several configurations which provide flexibility in the design used.

For isocyanate sampling, a solvent-free approach should be preferred to avoid all risks related to volatile solvents in the field. With that in mind, the CIP10 configuration using a centrifuged liquid medium originally designed for microbiologic (M) sampling was selected. The liquid medium would be replaced by a non-volatile co-solvent in which a derivatization agent would be introduced. During the sampling, the collected MDI aerosol would dissolve in the co-solvent and would be directly derivatized by the derivatization agent. The co-solvent

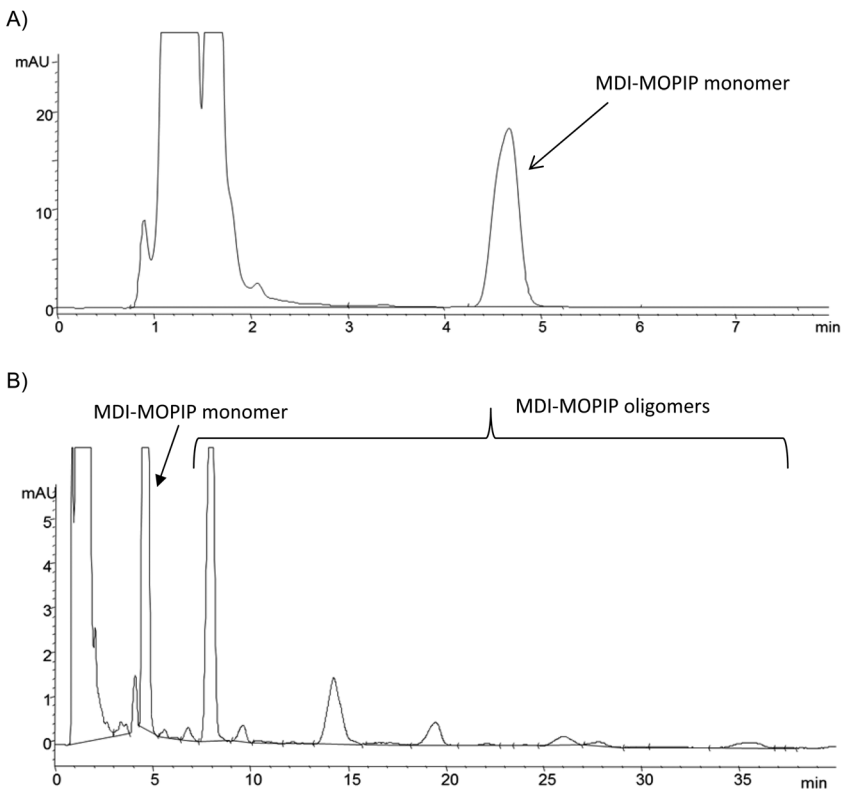

Fig. 1 (A) Chromatogram of the MDI–MOPIP monomer; (B) chromatogram of MDI–MOPIP oligomers.

selected for use in CIP10M was DMPS with the lowest viscosity commercially available to permit an efficient distribution inside the cup during centrifugation. Then, the derivatization agent MOPIP was selected due to its efficient reactivity with MDI[25] and its chromophore compatible with HPLC-PDA detection.[16,25] The use of MOPIP allows direct derivatization during sampling. The CIP10M device containing DMPS–MOPIP (0.5 mg MOPIP per mL DMPS) was characterized in the laboratory prior to any field evaluation to establish the performance that can be achieved for MDI. The results of this characterization are presented in the following paragraphs and a full laboratory validation of the analytical parameters is also included.

HPLC-PDA method for MDI–MOPIP monomer and oligomers

As a first step, MDI–MOPIP monomer and oligomers were spiked into pure ACN and analysed by HPLC-PDA[16,25] to ensure that the chromatographic separation was suitable for conducting subsequent experiments. Fig. 1 shows the MDI–MOPIP monomer and oligomer chromatograms obtained under the conditions used. As can be observed in this figure, good separation was achieved with all the substances and no chromatographic interferences were present. These conditions were judged satisfactory to initiate the development of the extraction procedure and the successive steps.

Extraction of the MDI–MOPIP monomer and oligomers from the DMPS medium

The development of an efficient extraction procedure is a mandatory step in achieving the established goal. The amount of extraction needed was optimized first. As an initial attempt, a known concentration (≈100% OEL) of the MDI–MOPIP monomer was spiked into pure DMPS. A negligible amount of MDI–MOPIP was detected after 4 extractions and most of the analyte was recovered in the three first extractions. Then, in another experiment, the extractions were repeated in parallel in pure DMPS and in DMPS containing 0.5 mg of MOPIP per mL and the results are presented in Fig. 2. As can be seen in this figure, the recovery of MDI–MOPIP was quantitative and the addition of MOPIP to DMPS had no negative impact on the extraction efficiency. A suitable recovery was obtained even in the presence of excess MOPIP. The same experiment was repeated with the MDI–MOPIP oligomers. As done previously, a known concentration (≈100% OEL; sum of the 6 major oligomers) of MDI–MOPIP oligomers was spiked into DMPS + MOPIP (0.5 mg mL^{-1}) and the results are shown in Fig. 3. As can be seen in this figure, a quantitative recovery was also obtained for the MDI–MOPIP oligomers. Finally, the extraction procedure was repeated at 3 different concentration levels for the MDI–MOPIP monomer and oligomers spiked into DMPS + MOPIP and the data are shown in Table 1. The MDI–MOPIP concentration had no impact on the extraction efficiency, and quantitative recoveries were obtained in all attempts. Based on these results, it was determined that 4 extractions were sufficient to recover the MDI–MOPIP monomer and oligomers, and that the next steps would use this efficient extraction protocol.

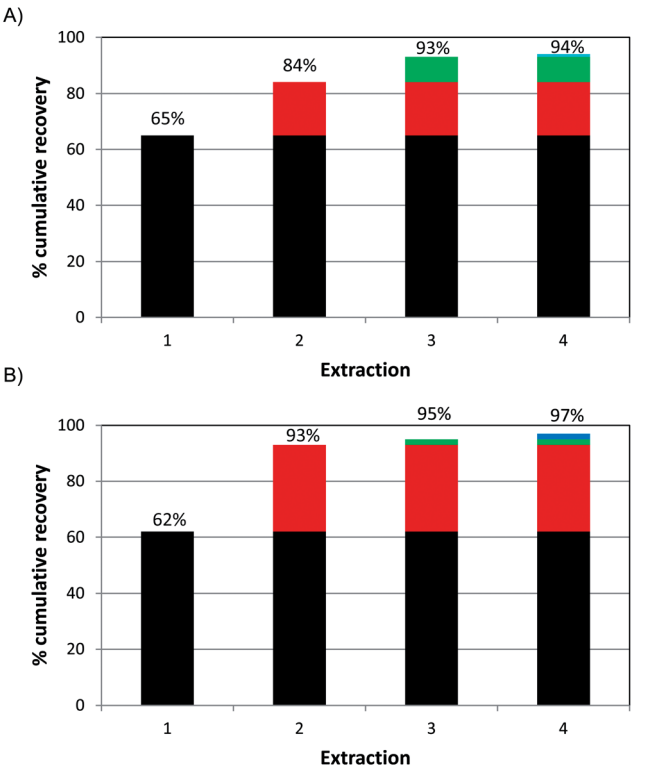

Fig. 2 Cumulative recovery of the MDI–MOPIP monomer in (A) DMPS; (B) DMPS + MOPIP.

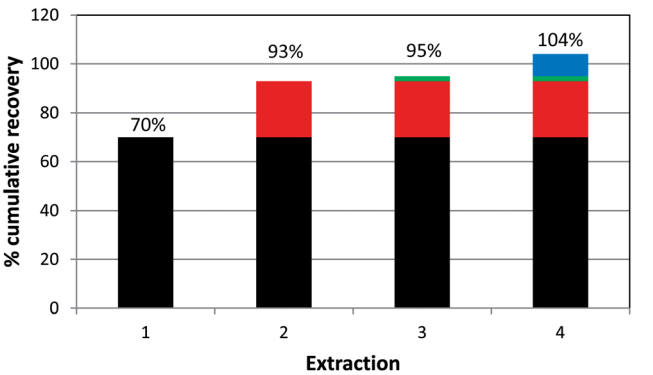

Fig. 3 Cumulative recovery of MDI–MOPIP oligomers in DMPS + MOPIP.

Reactivity of the MDI monomer and oligomers in DMPS

The use of DMPS must not prevent the reaction between free MDI and MOPIP. To assess the reactivity between free MDI and MOPIP in DMPS, a series of experiments were done in parallel. First, the CIP10M derivatization solution (DMPS + MOPIP) and the impinger derivatization solution (toluene + MOPIP) were placed in separate test tubes. Then, free MDI was spiked at a known concentration into both media. The results obtained with the impinger are considered as 100% reactivity. Fig. 4 shows the relative reactivity of the free MDI monomer in the CIP10M medium in parallel with the impinger medium. As can be seen in this figure, the reactivity of the CIP10M medium

Table 1 Recoveries of the MDI–MOPIP monomer and oligomers spiked at different concentrations in DMPS + MOPIP

	% Recovery	
Concentration spiked (% OEL)	MDI–MOPIP monomer	MDI–MOPIP oligomers
100	97 ± 2	104 ± 1
50	108 ± 3	107 ± 3
15	108 ± 3	102 ± 1

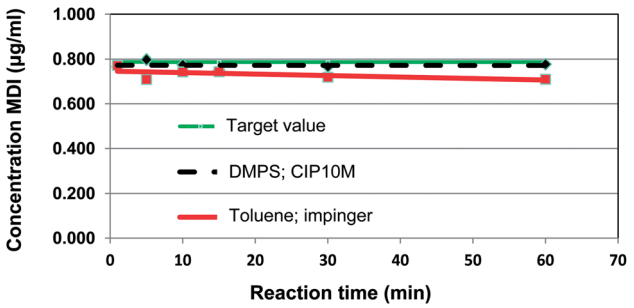

Fig. 4 Relative reactivity of the free MDI monomer in DMPS and in toluene.

(DMPS) was comparable to that of the impinger medium (toluene) at all the time points tested. The DMPS did not prevent the reaction between the free MDI monomer and the MOPIP. The experiment was repeated with the free MDI oligomers and the results are shown in Fig. 5. As can be seen in this figure, AA seems to interfere with the recovery of the MDI–MOPIP oligomers in DMPS, since lower amounts were detected than for toluene. However, removing AA from the experiment led to reactivity in the DMPS comparable to that for toluene, but no time course could be drawn as the reaction was never formally stopped. Nevertheless, the reaction seemed to occur very fast as the extraction procedure was performed 2 minutes after spiking. Based on these results, the addition of AA is avoided in the extraction procedure until the last step in order to obtain an optimal reactivity between the MDI oligomers and MOPIP and recovery. Under these conditions, comparable reactivity between the free MDI monomer and oligomers and MOPIP were obtained in DMPS and in toluene. This leads to the deduction that the CIP10M medium allows the same reactivity as the impinger medium. DMPS with MOPIP is a suitable medium to be used in CIP10M to collect the MDI monomer and oligomers.

Analytical performances

The samples were prepared using the extraction procedure developed above. The samples were extracted directly from the DMPS + MOPIP medium (0.5 mg mL^{-1}). The analytical performances are presented for the MDI–MOPIP monomer since the free MDI monomer is the constituent covered by the regulation. The oligomers should perform similarly based on the data obtained from the experiments presented above. Results for the oligomers would be reported as the total peak area detected and

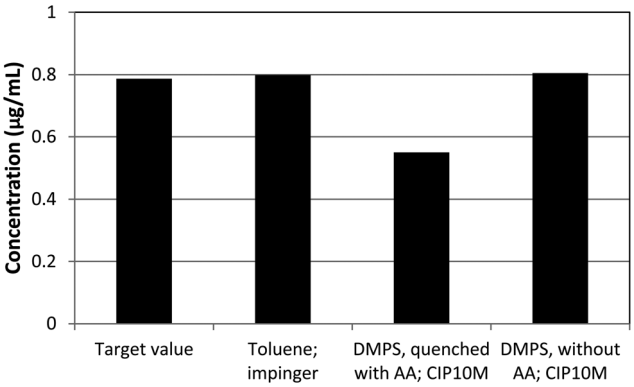

Fig. 5 Relative reactivity of free MDI oligomers in DMPS and in toluene.

quantified using the standard curve prepared with the MDI–MOPIP monomer since no individual pure MDI–MOPIP oligomer standards are available. Since the oligomers are in the same chemical family as the monomer, the chromophore should not be too different between the two analytes and it is assumed that a similar response factor should be obtained by UV detection.

Specificity and selectivity. The method's specificity and selectivity rely on the chromatographic retention times of the monomer and each oligomer and on the maximum wavelength used. To cause analytical interference, a substance must be collected by CIP10M, have the same retention time under the chromatographic conditions used, and have the same UV profile as the substances of interest. These conditions could occur, but are not favored. The specificity and selectivity were tested by analyzing several times the standard spiked in pure ACN and in the DMPS + MOPIP medium. No interferences were observed for any of the analytes.

Recovery and matrix effect. In addition to the experiments presented previously about the extraction efficiency, the recovery and matrix effect were formally investigated using the MDI–MOPIP derivative. Spiked concentrations in DMPS + MOPIP were compared to spiked concentrations in pure ACN and a total recovery of 98% was obtained, as shown in Table 2. This negligible matrix effect can be explained by the extraction used. The extraction is selective to the MDI–MOPIP derivative, thus minimizing the impact of the collection media on the analyte's signal because an almost pure analyte in ACN is injected into the system after extraction. These tests assessed only the extraction efficiency, as the derivatization efficiency was assessed earlier in separate experiments.

Carryover. A blank is injected after the highest concentration of the standard curve in each run to assess the potential carryover. No significant carryover was observed throughout the analysis.

Dynamic range, LOD/LOQ, precision and accuracy. The overall analytical performances of the method are presented in Table 3. The dynamic range was adjusted to cover the OEL with standards ranging from 0.079 µg mL^{-1} (10% OEL) to 0.787 µg mL^{-1} (100% OEL) with $R^2 \geq 0.990$. The LOD and the

Table 2 Recovery of the MDI–MOPIP monomer from the DMPS + MOPIP matrix

	Concentration ($\mu g\ mL^{-1}$)	0.079 $n = 6$	0.118 $n = 6$	0.197 $n = 6$	0.394 $n = 6$	0.787 $n = 6$
Spike in DMPS + MOPIP	Mean	0.072	0.112	0.187	0.374	0.769
	Standard deviation	0.002	0.005	0.004	0.008	0.034
	% CV	3%	5%	2%	2%	4%
Spike in pure ACN	Mean	0.071	0.121	0.189	0.389	0.767
	Standard deviation	0.002	0.003	0.006	0.008	0.014
	% CV	3%	2%	3%	2%	2%
	% Recovery	102%	92%	99%	96%	100%

Table 3 Analytical performances for the MDI–MOPIP monomer

Analytical parameters	MDI–MOPIP monomer
LOD	0.010 $\mu g\ mL^{-1}$
LOQ	0.033 $\mu g\ mL^{-1}$
Intra-day precision	4%
Inter-day precision	4%
Accuracy	100% ± 6%

LOQ are sufficient to meet expectations. The intra-day and inter-day precisions shown in Tables 4 and 5 are <6% for all the concentration levels tested, showing that the extraction procedure is robust and reliable in order to produce quantitative data. The accuracy was within an appropriate range of 100 ± 6% at a target level around 50% of the OEL. All these parameters validated the developed method and the extraction procedure. The overall method has been judged adequate to proceed with sampling activities. The application of this method to real samples can be initiated.

Proposed conditions for workplace sampling with CIP10M for MDI aerosols

Based on the results obtained in the laboratory so far, efficient collection is expected with CIP10M in the workplace for MDI aerosol sampling when using DMPS + MOPIP (0.5 $mg\ mL^{-1}$). To do the sampling, CIP10M must be filled with 2 mL of DMPS + MOPIP and kept vertical until the start. Once started, CIP10M can be moved in any direction as the liquid is kept inside the cup by centrifugation. CIP10M can be easily attached to a worker for personal sampling using a supplied shoulder strap. The CIP10M sampler was run for 8 hours in the laboratory and negligible loss of DMPS + MOPIP was observed. CIP10M must be returned to the vertical position at the end. Sampling rate calibration of the device should be performed at the beginning and at the end of the sampling period to ensure that 10 $L\ min^{-1}$ is used for sampling. The calibration can be done with a supplied portable calibration table. Following sampling, the extraction procedure will be applied to the DMPS + MOPIP medium, and HPLC-PDA analysis will be done on each sample. The results should be reported in $mg\ m^{-3}$.

Table 4 Intra-day precision for the MDI–MOPIP monomer

Concentration ($\mu g\ mL^{-1}$)	0.079 $n = 6$	0.118 $n = 6$	0.197 $n = 6$	0.394 $n = 6$	0.787 $n = 6$
Mean area	32	49	84	171	321
Standard deviation	1.5	1.6	3.7	7.2	12.8
% CV	5%	3%	4%	4%	4%

Conclusion

A new alternative has been developed to appropriately evaluate MDI aerosols in fast polymerization reaction processes. The method proposes CIP10M as the sampling device. A non-volatile co-solvent containing a derivatization agent is used as the collection medium. The medium composed of DMPS + MOPIP was developed. The use of MOPIP allows direct derivatization during sampling. The collected MDI is then analyzed by HPLC-PDA in the form of a MDI–MOPIP derivative. It has been demonstrated that the MDI–MOPIP monomer and oligomer derivatives can be quantitatively extracted from the DMPS + MOPIP medium. Moreover, the reaction efficiency between the free MDI monomer and oligomers and the MOPIP is not hindered by DMPS, and reactivity comparable to that for an impinger was obtained in the laboratory. The method's performance has been fully evaluated and the method is now ready to be tested in workplaces in order to be compared in real sampling situations to an impinger.

Table 5 Inter-day precision for the MDI–MOPIP monomer

Concentration ($\mu g\ mL^{-1}$)	0.079 $n = 6$	0.118 $n = 6$	0.197 $n = 6$	0.394 $n = 6$	0.787 $n = 6$
Mean concentration ($\mu g\ mL^{-1}$)	0.069	0.117	0.200	0.401	0.827
Standard deviation	0.0045	0.0030	0.0085	0.0198	0.0362
% CV	6%	3%	4%	5%	4%

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