The Analyst
FULL PAPER

Determination of airborne methyl isocyanate as dibutylamine or 1-(2-methoxyphenyl)piperazine derivatives by liquid and gas chromatography

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Received 5th July 2000, Accepted 29th August 2000
First published as an Advance Article on the web 2nd October 2000

The usefulness of a glass fibre filter method to collect airborne methyl isocyanate (MIC) was studied in laboratory experiments and in a workplace during manufacture of mineral wool insulation material. Filter collection was based on derivatisation *in situ* with 1-(2-methoxyphenyl)piperazine (2MP). 2MP impinger sampling was also evaluated in the workplace. Impinger sampling with dibutylamine (DBA) was used as an independent method. The samples were analysed by liquid and gas chromatography using various detection techniques: mass spectrometry, ultraviolet and electrochemical detection (LC-MS, LC-UV, LC-EchD and GC-MS). The sampling efficiency of 2MP filters for MIC varied with the origin of the glass fibre filter. Two Whatman filters (diameter 25 mm) with altogether 21 μmol of 2MP collected 100% of 9.8 μg of MIC during 30 min at an airflow rate of 1 l min^{-1}. The workplace measurements were performed at two concentration levels, 0.003 and 0.09 mg m^{-3}. The theoretical amounts of derivatisation reagent were 42 μmol (2MP filter), 52 μmol (2MP impinger) and 100 μmol (DBA). MIC concentrations were 20% lower by the 2MP methods compared with the DBA method (statistically significant difference). Breakthrough was 6% for the DBA method and 9% for the 2MP impinger method. To trap both MIC and isocyanic acid, which was also present in the workplace samples, a tenfold molar amount of 2MP reagent was used. The precision of sample preparation, expressed as relative standard deviation, was 3.5% (0.17 μg ml^{-1}, $n = 6$). The precision of sampling in the workplace was 15% (0.002 mg m^{-3}, $n = 6$). The limit of quantification was 0.0006 mg m^{-3} for 30 l of air by the 2MP impinger method and 0.03–0.05 mg m^{-3} by the 2MP filter method. Hence, airborne MIC can be determined using 2MP as derivatisation reagent. Impinger sampling is preferable when low concentration levels are expected.

Introduction

Isocyanates that contain the highly unsaturated N=C=O group are reactive with a host of compounds possessing an active hydrogen, *e.g.*, alcohols, phenols and amines. Aliphatic and aromatic diisocyanates are mainly used in the manufacture of polyurethanes for foams, elastomers, coatings and adhesives. Monoisocyanates are predominantly used as intermediates in the manufacture of certain agricultural and pharmaceutical products, *e.g.*, herbicides, insecticides and oral hypoglycaemic agents.[1] Methyl isocyanate (MIC), an aliphatic monoisocyanate, can be formed during thermal (200–300 °C) decomposition of certain substances containing organic bonded nitrogen.[2] MIC has also been found in mainstream cigarette smoke at concentrations of 1–5 ppm.[3]

A method for determining airborne MIC has been published by OSHA.[4] The method is based on sampling with 1-(2-pyridyl)piperazine-coated XAD-7 tubes and analysis by liquid chromatography (LC) using fluorescence or ultraviolet (UV) detection.[4] Karlsson *et al.* reported sampling of MIC by an impinger method using dibutylamine (DBA) as derivatisation reagent, followed by quantification by LC mass spectrometry (MS).[2] A fluorimetric method has also been published recently.[5]

There are numerous methods for determining diisocyanates and their oligomers. They have been critically reviewed by Levine *et al.* and Streicher *et al.*[6,7] Both impinger and filter methods can be used to collect volatile diisocyanates like toluene diisocyanate efficiently.[6] In many countries, including Finland, a method for determining diisocyanates, based on derivatisation with 1-(2-methoxyphenyl)piperazine (2MP), is used.[8] This method uses UV or electrochemical detection (EchD) and was developed by the Health and Safety Executive in the UK to determine the total reactive isocyanate group. The sampling device consists of an impregnated filter or a toluene impinger solution, to which a back-up filter impregnated with 2MP can be connected to collect aerosols more efficiently.

Phenol–formaldehyde–urea resins are commonly used as binder in mineral wool insulation materials. As the resins are polymerised at about 250 °C, MIC may be generated in the work environment. The Finnish occupational exposure limit value (15 min short-term limit) for isocyanates is 0.035 mg m^{-3} expressed as isocyanate groups. This value corresponds to 0.049 mg m^{-3} calculated as MIC. Hence, MIC concentrations of 0.005 mg m^{-3}, corresponding to 1/10 of the isocyanate limit value, need to be determined. For a short-term sample, sufficient sensitivity requires flow rates of about 1 l min^{-1}, which can be applied to both impinger and filter sampling. Impinger sampling, however, is cumbersome in assessing a worker's personal exposure to inhalable chemicals.

The aim of the present study was to evaluate the usefulness of the 2MP filter method for collecting airborne MIC. The 2MP filter method was tested in the laboratory and in a workplace during manufacture of mineral wool insulation material. 2MP impinger sampling was also evaluated in the workplace. Impinger sampling with DBA as derivatisation reagent was used as an independent method. A secondary aim was to compare different chromatographic techniques to determine

DOI: 10.1039/b005388k

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MIC. We report results from determinations using LC-MS, LC-UV, LC-EchD and gas chromatography-mass spectrometry (GC-MS).

Experimental

Apparatus

LC-MS. A single quadrupole mass spectrometer (Waters Platform LCZ MS Detector, Manchester, UK) was used in the electrospray mode monitoring positive ions. The cone voltage was 40 V, and the temperature of the ion source was 110 °C. The mass spectrometer was connected to a Waters Alliance 2690XE separation module consisting of a quaternary solvent delivery system, a refrigerated, integrated autosampler, a column heater and a variable volume injection system (Waters, Milford, USA).

The MIC–DBA derivative was determined using a mobile phase of acetonitrile–water (1 + 1) containing 0.5% formic acid. The flow rate was 0.2 l min^{-1}. The LC column was Hypersil (Astmoor, Runcorn, Cheshire, UK; Quest 150 × 2.1 mm id, 5 μm, HyPURITY™ C18). The column temperature was 30 °C. The autosampler temperature was 4 °C. The MIC–DBA derivative eluted at 4.8 min and the DBA derivative of the ethyl isocyanate (EIC) internal standard at 6.1 min.

LC-UV-EchD. The 2MP samples from the laboratory tests for the determination of sampling efficiency were analysed using a liquid chromatograph (Hewlett Packard HP 1100, Waldbronn, Karlsruhe, Germany) equipped with an autosampler and a variable injection loop. A Hewlett-Packard photodiode array detector (HP 1090) coupled in series with an electrochemical detector (HP 1049A) was used to detect the MIC-2MP derivative. The signals were recorded with the HP Chemstation. UV detection was performed at 245 nm. The injection volume was 10 μl. The compounds were separated on a Ultrasphere (Beckman, Fullerton, CA, USA) 5 ODS IP column (250 mm × 4.6 mm id), using acetonitrile–water with sodium acetate 1.0 g l^{-1} (0.32 + 0.68) at pH 6 as a mobile phase at a flow rate of 1 ml min^{-1}. The 2MP derivative of MIC eluted at 6.2 min immediately before the reagent peak.

The 2MP samples from workplace air were analysed using an LC system comprising two Waters 510 pumps, a Waters 717 plus autosampler, a Waters 996 photodiode array detector and a Waters 464 electrochemical detector (Waters, Milford, USA). The system was piloted by a workstation equipped with Millenium software. During the chromatographic run, UV spectra ranging from 230 to 280 nm were monitored, with extraction of the 245 nm peak for quantification. The compounds were separated (10 μl injected) on a Ultrasphere 5 ODS IP column (250 mm × 4.6 mm id), using acetonitrile–water with sodium acetate 2.2 g l^{-1} (0.3 + 0.7) at pH 6 as a mobile phase at a flow rate of 1 ml min^{-1}. The 2MP derivative of MIC eluted at 8.9 min immediately before the reagent peak.

In both systems, the electrochemical detector was operated at +0.8 V at ambient temperature in the 100 nA range (Waters) or the 500 nA range (HP).

The response of MIC–2MP was linear over the range 0.02–50 μg ml^{-1} with the UV detector and 0.01–1 μg ml^{-1} with the Ech detector.

GC-MS. The GC-MS equipment consisted of a Hewlett Packard 5989A mass spectrometer (Palo Alto, California, USA) connected to a Hewlett Packard 5890 Series II capillary gas chromatograph equipped with a Hewlett Packard 7673 autosampler (Hewlett Packard, Little Falls, Willmington, DE, USA). Ionisation was achieved using the electron impact mode (70 eV). The transfer line, source and quadrupole temperatures were 250 °C, 300 °C and 100 °C, respectively. Separation was achieved on an open tubular fused silica capillary column (50 m × 0.2 mm id) coated (0.11 μm film thickness) with 5% phenylmethylsilicone (cross-linked, Hewlett Packard). The column temperature program was 115 to 200 °C at 20 °C min^{-1}. The carrier gas was helium with a linear gas velocity of 22 cm s^{-1}. The injector was operated in the splitless mode at an inlet temperature of 115 °C and a splitless period of 30 s. The MIC–DBA derivative eluted at 8.8 min and the DBA derivative of the butyl isocyanate (BIC) internal standard at 11.3 min. The response of MIC–DBA was linear over the range 0.02–50 μg ml^{-1}.

Chemicals

The solvents used in the experiment were toluene (analytical reagent grade, Merck, Darmstadt, Germany or Baker, Gross Gerau, Germany), acetonitrile (HPLC grade S, Rathburn, Walkerburn, Scotland, UK), acetic anhydride, sodium acetate, glacial acetic acid and formic acid (all analytical reagent grade, Merck). MIC (1 mg ml^{-1}, purity 98%) was bought from Chem Service Inc. (West Chester, PA, USA), EIC (98%), BIC (98%) and 2MP (98%) from Aldrich (Beerse, Belgium) and DBA (99%) from Fluka (Buchs, Switzerland). Water was purified by means of Milli-Q-academic and Elix S. The following glassfibre filters free from organic binders were tested: Sartorius (25 mm), Millipore (24 mm) and Whatman (25 mm). Teflon wool was from Alltech Ass., Applied Science Labs, Deerfield, IL, USA.

Sampling of workplace air

The glass fibre filters were impregnated with 400 μl of toluene containing 2MP at 52 mmol l^{-1}. Two filters were placed in the filter holder. The impinger flasks were filled with 10 ml of toluene containing either DBA at 10 mmol l^{-1} or 2MP at 5.2 mmol l^{-1}. The theoretical amounts of derivatisation reagent were thus 42, 100 and 52 μmol, respectively. Air was pumped through the filter and impingers with MSA (Mine Safety Appliances, Pittsburgh, PA, USA) or Ametek (Paoli, PA, USA) pumps at an airflow rate of about 1 l min^{-1}. The pumps were calibrated in the laboratory before sampling for accurate flow rates and checked afterwards. The air sampling was performed at two concentration levels with six replicates of each sampling device at a factory which produced insulation material from mineral wool, using phenol–formaldehyde–urea resin as binder. The urea is the source of nitrogen. At each site, the three different sampling devices were placed in pairs as close to each other as possible (within an area measuring 30 cm × 60 cm) and at the same height (1 m). The sampling time was 50 min at a site with expected high concentration and 90 min at a site with expected low concentration.

Work-up and quantification by LC-MS

A known amount (1.8 μg) of EIC (internal standard) was added to the DBA sampling solution and to the MIC–DBA external standards that were prepared *in situ*. EIC was allowed to react with DBA for at least 30 min. Then aliquots, typically 2 ml, were taken for analysis. The toluene was evaporated to dryness under a gentle stream of nitrogen. The samples were reconstituted in 1 ml of acetonitrile. Five different concentrations of MIC, 0.1–5 μg per sample, were used for the calibration curve. Sample, standard or blank (8 μl) was injected for analysis. The analyte was quantified by monitoring protonated molecular ions. The protonated ions to be used were determined by scanning mass spectra from *m/z* 100 to *m/z* 600. The ions at the

apex of the peaks in the scan mode were then used in the selected ion recording mode. The limit of quantification of MIC was 8 pg per 8 μl injection.

Work-up and quantification by LC-UV-EchD

The 2MP filter samples (two filters per sample) were immersed in 3 ml of acetonitrile immediately after sampling at the workplace. Before analysis, 10 μl of acetic acid anhydride was added and the sample vial placed in an ultrasonic bath for 10 min, after which the sample solution was passed through a filter (0.45 μm Millex HV type, Millipore). To 1 ml of the 2MP impinger solution was added 10 μl of acetic acid anhydride, and the toluene was evaporated to dryness under a gentle stream of nitrogen. If a concentration step was needed, 100 μl of acetic acid anhydride was added to 10 ml of the 2MP impinger solution. The residue was reconstituted in 1 ml of acetonitrile. The analyte was quantified by the external standard method using five different concentrations in the range 0.15–6 μg per sample. The quantification limit for MIC prepared in 2MP impinger solution was 0.4 ng at an injection volume of 20 μl. Because of severe background interference originating from the filters, the detection limit achieved with the filter technique was tenfold that achieved with the impinger solution.

Work-up and quantification by GC-MS

An aliquot, typically 1 ml, of the DBA sampling solution was evaporated to dryness and reconstituted in 1 ml of toluene. When needed, a five- to ten-fold concentration step was introduced, *e.g.*, 5 ml of the sampling solution was evaporated and reconstituted in 0.5–1 ml of toluene. Sample solution (1 μl) was injected and analysed in the selected ion monitoring mode. The analyte was quantified by the internal standard method using BIC as internal standard (10 μg ml^{-1}). The ions monitored were *m/z* 186 (molecular ion) and *m/z* 143 ($M–C_3H_7$) for MIC and *m/z* 228 (molecular ion) and *m/z* 185 ($M–C_3H_7$) for BIC. Five standards were prepared in the range 0.02–2 μg ml^{-1}. Response factors were calculated for both ions for MIC, and quantification was done with both. The average of these results is reported. The limit of quantification was 50 pg per 1 μl injection. The GC-MS technique was used to study the stability of the MIC–DBA derivative.

Testing of the sampling efficiency of 2MP filters in the laboratory

The test system was similar to that described by Andersson *et al.*[9] and produced air with a known flow rate and of known relative humidity (RH). Synthetic air (AGA, Helsinki, Finland, purity 99.99%) was humidified in gas dispersion bottles and diluted with dry air in a mixing chamber (1.0 l) containing an RH meter (Vaisala Humicap HMI II). In the recovery experiment, the humidified air was divided into seven equal parts flowing through seven parallel collection devices. Each collection device consisted of one glass fibre filter (Sartorius or Millipore) or two glass fibre filters (Whatman), each impregnated with 200 μl of a 10 mg ml^{-1} solution of 2MP.[8] The filters were freshly prepared and packed in Millipore filter cassettes. Each collection device, which also included a back-up sampler, was coupled to an injection port *via* a short (50 mm) glass tube containing Teflon wool. Sampling was performed at 20% and 80% RH at an airflow rate of 1 l min^{-1} (0.93–1.07 l min^{-1}).

With the airflow on, 5 μl of toluene containing 3.9 μg of MIC (10 μl of toluene containing 9.8 μg of MIC for the Whatman filters) was injected *via* the injection port into the Teflon wool in the glass tube, from which it evaporated onto the filters. Sampling efficiency was calculated as the mean value of 4–6 parallel collections. A seventh collection performed with only toluene was used as a blank. The total air volume was 15–19 l for the test with 3.9 μg of MIC and 30–33 l for 9.8 μg of MIC.

The filters were kept at room temperature for about two hours and then desorbed with 2 or 3 ml of acetonitrile. One batch was kept in the refrigerator for one week before desorption. Before analysis 10 μl of acetic anhydride was added, and the samples were kept in an ultrasonic bath for 10 min. Impregnated filters spiked with external standards were used to determine the sampling efficiency of the filters for MIC.

Stability of the DBA and 2MP derivatives of MIC

The stability of the MIC–2MP derivative was studied in groups of six samples at two levels, 1 and 10 μg per filter stored at +4 °C for up to two weeks (four, seven and 14 days). This storage test was carried out for the derivative in acetonitrile, toluene or on dry glass fibre filters. The acetonitrile solution represented the initial calibration curve derived from MIC-spiked 2MP impinger solution in toluene and subsequently prepared for LC analysis. The storage test in toluene was done to simulate the storage of an impinger sample. In addition, the stability of the MIC–DBA derivative at eight different concentrations ranging from 0.05 to 4.0 μg ml^{-1} in toluene was evaluated. The storage temperature was −20 °C and the storage times 14, 21 and 28 days.

Statistical analysis

The results from the laboratory experiments were tested for the effects of humidity and filter type by a two-way analysis of variance. The *F* test was used to determine the influence of measurement site. The potential discrepancy between the DBA samplers (impinger) and the 2MP samplers (filter and impinger) was tested by paired *t* tests (log-transformed values).[10]

Results

Desorption efficiency of MIC from spiked 2MP filters

Desorption efficiency (%) of MIC from spiked 2MP filters was determined by comparison with 2MP–toluene spiked with MIC standards. The Millipore filters were studied at levels of 1 and 10 μg per filter with six replicates. The desorption efficiency was 80% ± 6% (*s*) for both concentrations. The Sartorius and Whatman filters were evaluated at levels of 0.5 and 5 μg per filter, also with six replicates. The desorption efficiencies for Sartorius filters were 66% ± 14% (*s*) for 0.5 μg per filter and 94% ± 5% (*s*) for 5 μg per filter. The desorption efficiency for Whatman filters was 85% ± 5% (*s*) for both levels.

Sampling efficiency of 2MP filters

The effects of air humidity and filter storage on the sampling efficiency for MIC of the different types of filter are presented in Table 1. The sampling efficiency for the Sartorius and Millipore samplers (one filter per holder) was 78–85% at 20% RH and 65–83% at 80% RH. The proportion of MIC in the back-up sampler was greater than 10% for both filter types. For the Whatman sampler (two filters), breakthrough was less than 1.2% and sampling efficiency close to 100% at both 20% and 80% RH. The difference in sampling efficiency was statistically significant ($F(2,26) = 50.7$, $P < 0.001$) between the Whatman and Sartorius filters on the one hand and the Millipore filters on

the other. MIC sampling efficiency, for all filter types, was significantly lower at RH 80% compared with RH 20% ($F(1,26) = 6.2$, $P < 0.02$).

Stability of the DBA and 2MP derivatives of MIC

The MIC–2MP derivative was stable in acetonitrile and only a slight decline, 1–1.5%, was observed in toluene at +4 °C for up to two weeks. MIC–2MP was not stable on dry filters at 1 μg per filter. The degradation was 17% and 20% after four and 14 days, respectively. At the 10 μg per filter the degradation was 2% after four and 6% after 14 days.

The DBA derivative of MIC stored in toluene for 14 days at −20 °C showed a degradation of 3%. A 6% reduction was observed after 21 and 28 days of storage. These measurements were carried out using the GC-MS technique.

Stability of pure MIC in toluene

The pure MIC standard in 5 ml of toluene was received in sealed glass ampoules. After the seal had been opened to prepare the first set of standards, the remaining MIC solution was transferred to glass vials, the vials were sealed with Teflon–silicone-lined crimp seals and subsequently stored at −20 °C. After one month and six months, new sets of standards were prepared. Compared with the first set of standards, the response was 95% after one month and 70% after six months. The response was about 20% lower when Teflon–red rubber-lined seals were used. The GC-MS technique was used for these tests.

Workplace measurements

The results of the workplace measurements are shown in Table 2. At the higher concentration level, the concentrations obtained by the 2MP methods were about 80% of that by the DBA method. Back-up impingers and filters were used to check for breakthrough. The breakthrough was 6% with the DBA impinger and 9% with the 2MP impinger. The breakthrough with the filter method could not be determined, as the amount of MIC on the back-up filters was below the detection limit. At the lower concentration level, the concentration obtained by the 2MP impinger method was also 80% of that by the DBA method. The lower concentration level was below the limit of detection for the 2MP filter method. The difference between the DBA method and the 2MP methods was significant within the 95% confidence interval. Analysis of the influence of the site yielded the following results for the independent (DBA) method: $F(5,5) = 7596$, $P < 0.001$. The corresponding F test result for the 2MP impinger method was $F(5,5) = 6548$, $P < 0.001$.

Precision of sample preparation

The precision of sample preparation expressed as the relative standard deviation (RSD) for six replicates was 3.4% with UV detection and 3.9% with EchD. The concentration of MIC in the workplace-derived 2MP impinger sample, which was used for the determination, was 0.17 μg ml^{-1} corresponding to 0.03 mg m^{-3} for a 45 l air sample. For comparison, the precision of six replicate injections of a standard solution (0.5 μg ml^{-1}) was 1.0% by UV detection and 2.8% by EchD.

Discussion

Guidelines for the development and evaluation of air sampling and analytical methods have been published by NIOSH.[11] There is also a European standard (EN 1076)[10] describing test methods for pumped sorbent tubes for the determination of gases and vapours, based on dynamic generation of known test vapours into an exposure chamber. However, because MIC is an extremely noxious, very reactive and highly volatile compound, it is not advisable to produce a dynamic atmosphere of MIC. Therefore, we chose to generate test vapours of MIC by injecting known amounts in toluene solution into Teflon wool placed in a short pretube. The detection limit for the studied filters was 0.2 μg per sample, corresponding to 0.013 mg m^{-3} for a 15 l sample, which is about one-fourth of the Finnish 15-min limit value. The injected amounts, 3.9 and 9.8 μg were chosen to allow reliable determination of breakthrough from the back-up filters.

In the initial experiments with Millipore and Sartorius glass fibre filters, the total recoveries were over 89%. Nevertheless,

Table 1 MIC sampling efficiency of 2MP-impregnated glass fibre filters (I) with back-up filters (II) at two levels of RH

Filter	Amount of MIC/μg	RH (%)	n	Recovery (%)[a] Filter holder I	Filter holder II	Total recovery ± s (%)
Sartorius	3.9	20	6	84.8	20.3	105.1 ± 4.0
		80	4	82.6	16.4	98.9 ± 7.3
Sartorius[b]	3.9	20	6	81.6	12.0	93.6 ± 7.9
		80	6	81.2	31.3	112.4 ± 9.5
Millipore	3.9	20	6	77.9	15.9	93.7 ± 4.0
		80	4	64.8	24.2	89.0 ± 9.2
Whatman[c]	9.8	20	6	101.4	⩽1.2	101.6 ± 3.1
		80	6	98.8	1.1	99.9 ± 5.1

[a] Sampling efficiency was calculated as the mean value of 4–6 replicates analysed by LC-UV. [b] The filters were kept in the refrigerator for one week before desorption. [c] Two filters per holder, EchD.

Table 2 MIC concentrations in workplace air during manufacture of mineral wool insulation material

Measurement site	MIC concentration, mean ± s (RSD in parentheses)[a]/mg m^{-3} DBA impinger[b]	2MP impinger[c]	2MP filter[c]
High-concentration site	0.086 ± 0.023 (27%)	0.068 ± 0.021 (31%)	0.069 ± 0.023 (33%)
Low-concentration site	0.0025 ± 0.0003 (12%)	0.0020 ± 0.0003 (15%)	Below detection limit

[a] Mean value of six parallel samples. [b] LC-MS. [c] LC-UV.

the first pilot measurements with Sartorius and Millipore filters in the workplace showed unacceptably high breakthrough. For the Sartorius filter, the breakthrough was over 50%. The probable reason for this was the presence of isocyanic acid (ICA) in the workplace air. The identity of ICA was tentatively confirmed by both GC-MS and LC-MS in the scan mode. ICA, which could not be quantified for lack of standard, is presumably more reactive than MIC and evidently competed with it, preventing most of the MIC from reacting with 2MP during sampling. The Millipore filters, which were stored for four months before sampling, failed to collect MIC from the workplace atmosphere. The LC-chromatograms of the workplace samples showed the presence of 2MP, indicating stability of the reagent. Moreover, the filters worked well in the laboratory when preparing spiked calibration standards. The reason for the unsuccessful sampling remained unresolved.

After the experience of the pilot study, we decided to perform laboratory tests with two filters per holder, thus doubling the amount of reagent. Furthermore, these tests were done with Whatman filters which were thicker and more porous than Sartorius or Millipore. The sampling efficiency for 9.8 μg of MIC was close to 100% with almost negligible breakthrough (Table 1). The workplace evaluation was done at two sites, one with medium to high and one with low MIC concentrations, chosen according to the tentative results from the pilot study. According to the NIOSH guidelines[11] and the EN 1076 standard,[10] both area samples and personal samples should be included in the field evaluation of a method. For practical reasons, only area sampling was performed in the present study. The 2MP impinger and filter methods yielded approximately 20% lower concentrations compared with those obtained by the DBA method. The precision of the measurements was about 30% for all methods at the high-concentration site. At the low-concentration site the precision was better, 15%, but here results were obtained only for the impinger methods. It is noteworthy that the concentration of MIC at the low-concentration site was below the detection limit of the filter method. To ensure the presence of a sufficient amount of reagent, the filters were impregnated with a double amount of reagent, theoretically 42 μmol of 2MP per sampler. Although the laboratory experiments had yielded acceptable results with the high amount of 2MP, the workplace samples contained impurities eluting close to MIC, which hampered the chromatography and affected the detection limit of the method. At the high-concentration site, there was some breakthrough with both impinger methods, 6% with the DBA and 9% with the 2MP method.

The relative difference in the reactivity of the DBA and 2MP reagents, which might explain the discrepancy of results in the present study, has been studied previously.[12,13] The reaction rates of aliphatic diisocyanates were studied by mixing isocyanate with an excess of DBA or 2MP in toluene, and the amount of the derivative was measured at appropriate intervals.[12] The result showed that DBA reacted 2–3 times faster than 2MP. In another study, equimolar mixtures of DBA and 2MP were used to calculate partial rate factors of the reagents for some diisocyanates.[13] According to the latter study, 2MP was 1.2–1.5 times faster than DBA. In our study, the molar concentration of 2MP was about half that of DBA. Even at the high-concentration site, the molar amount of 2MP was over 10 times that required to trap MIC and ICA simultaneously. This was estimated by quantifying ICA against MIC.

The statistical analysis showed that the poor precision at the high-concentration site was due to differences in workplace air compared with the low-concentration site and not to differences in the sampling methods. The individual MIC concentrations varied widely within this site, which was as small as possible (30 cm × 60 cm). Because of the poor precision at the high-concentration site, all results were treated as data pairs by pairing samplers of the tested methods with the nearest samplers of the independent method. This analysis revealed that the consistently lower concentration levels obtained by the 2MP methods compared with the DBA method constituted a statistically significant difference within the 95% confidence interval. This result would appear to indicate that neither of the 2MP methods fulfil the accuracy criterion of a maximum of 10% bias, provided that the DBA method gives accurate results. However, the reasons for the significant difference between the methods may be found in bias of the independent method.

The independent (DBA) method is also subject to errors, especially as the MIC–DBA derivative is semivolatile. As the DBA method includes a concentration step by evaporation to dryness, and as the volatility of the internal standard EIC is slightly different, it does not fully compensate for evaporation losses. The areas of the EIC internal standards were also consistently lower in the MIC external standards than in the workplace samples. A calculation by means of external standards resulted in about 60% higher MIC concentrations than did calculation with internal standard. Possibly the excess of ICA in the workplace samples reduced the losses of MIC and the internal standard during evaporation by decreasing their partial vapour pressures. To compensate for evaporation losses of the standards, it might be feasible to simulate conditions in the field by adding a correspondingly high standard concentration of ICA–DBA. This assumption should be tested as soon as the derivative is commercially available.

The highest measured concentrations of MIC were about 0.1 mg m^{-3}, with less than 10% in the back-up impinger after 50 min of sampling. This means that the 2MP samplers have enough capacity (about 50 μmol of 2MP) to collect MIC quantitatively in the presence of excess ICA during 30 min at concentrations 4–5 times the exposure limit value. With the 2MP impinger method, MIC concentrations of about 5% of the present limit value could be detected reliably. The quantification limit for a 30 min sample is about 0.0006 mg m^{-3}, which makes the method sensitive enough for determination of airborne MIC during processes where excess of ICA is formed. The 2MP filter method can be used to detect MIC at higher concentration levels. It should also be noted that the GC-MS technique proved to be a valuable alternative to the LC-MS technique for the determination of the MIC–DBA derivative.

The MIC–DBA and MIC–2MP derivatives were stable in acetonitrile (MIC–2MP) or toluene solution (MIC–DBA and MIC–2MP) at −20 °C for up to two weeks. MIC–2MP is not stable on dry filters, especially at levels of 1 μg or less per filter. Because the initial storage studies on dry Millipore filters were discouraging, no further tests were done with the other types of filter. We recommend that filter samples be desorbed immediately after sampling in the workplace and that the analysis be carried out within two weeks. To ensure constancy of the analytical responses to the MIC derivatives, it is advisable to open a new glass ampoule of pure MIC standard for every new set of samples.

In summary, airborne MIC can be determined using 2MP as derivatisation reagent. Impinger sampling is preferable when low concentration levels are expected. The 2MP reagent yields approximately 20% lower concentration values than does the DBA reagent during the applied conditions.

We thank Tuike Nenonen and Pirjo Toropainen for skilful technical assistance. We also gratefully acknowledge the contribution of Jaana Pentti who carried out the statistical analyses.

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