

Determination of hexamethylene diisocyanate-based isocyanates in spray-painting operations

Part 2.† Comparison of high performance liquid chromatography with capillary zone electrophoresis

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A capillary zone electrophoresis (CZE) approach was developed for the determination of hexamethylene diisocyanate (HDI) monomer and HDI-based oligomers. A comparison of CZE with high performance liquid chromatography (HPLC) indicates that the CZE separation completely isolates isocyanates from excess solvent, derivatizing reagent and pigment while offering a fivefold increase in sensitivity. The CZE approach allows for the quantification of HDI monomer and oligomer within a 1 min time window under the run conditions selected. For the determination of HDI-based oligomer, provided that the relative response with respect to HDI monomer is calculated, there is no significant difference ($p < 0.05$, $n = 10$) in the isocyanate air concentration when using either HPLC or CZE. The results are significant because they indicate that CZE has advantages for the determination of both HDI-based oligomer and HDI monomer generated during spray-painting operations.

Introduction

Isocyanates are a significant hazard in the workplace.¹⁻⁷ Workers who are involved in the production of polyurethane foams, elastomers and fibers and in the application of polyurethane paints and coatings are all exposed to diisocyanate and polyisocyanates. These compounds irritate the nose, throat and lungs and may eventually lead to the development of bronchial asthma.²⁻⁶

A number of methods have been developed for the sampling and determination of atmospheric organic isocyanates.⁸⁻¹⁰ The Occupational Safety and Health Administration (OSHA) prescribes a protocol for sample collection on a filter followed by high performance liquid chromatography (HPLC).¹¹ The National Institute for Occupational Safety and Health (NIOSH) promulgates Method 5521¹² for the determination of isocyanates in the USA. This method is an adaptation of MDHS 25, Method for Total Isocyanate in Air, developed for use in the UK.¹³ The last two methods use an impinger filled with 1-(2-methoxyphenyl)piperazine (MOP) in toluene for sample collection followed by HPLC analysis.

In this work, we developed and validated a capillary zone electrophoresis (CZE) approach to the determination of total HDI-based isocyanates, since CZE has several advantages relative to HPLC: low solvent consumption, a relatively short analysis time and higher resolution.¹⁴ This work extends our previous efforts to find analytical approaches to the determination of isocyanates when collected on polyurethane foam (PUF)-based samplers.¹⁵

Experimental

Reagents

1-(2-Methoxyphenyl)piperazine (MOP) was obtained from Fluka (Milwaukee, WI, USA), HDI monomer (HDI) from

Eastman Kodak (Rochester, NY, USA), Desmodur N-100 (N-100), which contains 99.3% polyisocyanate (predominately in the form of the biuret trimer of HDI), from Bayer Chemical (Pittsburgh, PA, USA),¹⁶ dimethyl sulfoxide from Aldrich (Milwaukee, WI, USA), acetonitrile (HPLC grade) and methanol from EM Science (Gibbstown, NJ, USA), acetic anhydride, glacial acetic acid, toluene and anhydrous sodium acetate from Fisher (Fairlawn, NJ, USA) and phosphoric acid and sodium phosphate from Baker (Phillipsburg, NJ, USA).

Preparation of HDI-MOP and N-100-MOP standard solutions

Isocyanate-MOP standards were prepared by directly reacting HDI-based isocyanates (which contain the NCO moiety) with MOP (which contains an accessible amine group) to form ureas (containing the -NCON- moiety), as described in NIOSH Method 5521.¹² A stock standard solution containing 500 μM HDI-MOP was prepared by dissolving 27.6 mg of HDI-MOP in 100.0 ml of methanol. A stock standard solution of N-100-MOP containing 1200 μmol of isocyanate groups per liter was prepared by dissolving 158.1 mg of N-100-MOP (equivalent mass of Desmodur N-100 = 191) in 100.0 ml of methanol. A 1000 mg l^{-1} MOP stock standard solution was prepared by dissolving 0.100 g of MOP in 100 ml of methanol.

In order to compare CZE with HPLC, five working standard solutions, containing final concentrations of 2.5–40 μM of HDI-MOP (5–80 μM NCO), 2.0–32 μmol of isocyanate groups per liter of N-100-MOP (6.0–96.0 μM NCO) and 10 mg l^{-1} MOP, were prepared by mixing the appropriate amount of a 500 μM HDI-MOP stock standard solution and 1200 μmol of isocyanate group per liter N-100-MOP stock standard solution with 0.1 ml of a 1000 mg l^{-1} MOP stock standard solution and then diluting to 10 ml with methanol. To half of each standard solution 10 μl of acetic anhydride were added.

For the analysis of samples obtained during spray-painting operations, at least six working standard solutions were prepared. These HDI-MOP standard solutions contained 20 μl

† For Part 1 see ref. 15.

of acetic anhydride, 100 mg l⁻¹ of MOP and 0.25–16 mg l⁻¹ of HDI–MOP in methanol.

In order to identify polyisocyanates generated during spray-painting operations, a 50 µl portion of the isocyanate hardener (bulk catalyst) was diluted in 10 ml of toluene and 50 µl of this solution were then diluted to 10 ml with 1000 mg l⁻¹ MOP in toluene. The solution was allowed to react for 12 h before heating to dryness under a gentle stream of nitrogen. A 30 µl aliquot of acetic anhydride was added to the dry residue, which was reconstituted in 5 ml of methanol while agitating the solution in an ultrasonic water-bath for 15 min.

The preparation of methoxyphenylpiperazine derivatives was performed in a fume-hood in order to avoid exposure to isocyanate and solvent vapors. Isocyanates are known respiratory irritants.

Preparation of sponge samplers

The polyether-based polyurethane foam (PUF) sponge (No. 2405; Supelco, Bellefonte, PA, USA) was cut to the correct thickness using a razor blade. Sponges for use in the IOM sampler (SKC, Eighty Four, PA, USA) were 15 mm thick and sponges for use in the cassette sampler (Nuclepore, Pleasanton, CA, USA) were 17.5 mm thick. The sponges for both types of samplers were then punched from the slice using a No. 15 cork borer (23 mm id). The sponges were soaked in dimethyl sulfoxide for at least 2 h before extracting three times with 10 ml of acetonitrile, then air drying. Glass-fiber filters (25 mm) (Omega, Chelmsford, MA, USA) were impregnated with 50 mg l⁻¹ MOP in acetonitrile, then air dried.

The cassette samplers were assembled by placing an aluminum mesh screen (2.5 cm in diameter) in the bottom of the cassette sampler, followed by the impregnated glass-fiber filter, then the clean sponge on top. The IOM samplers were assembled by placing the impregnated glass-fiber filter in the bottom, then positioning the sponge on top before screwing the cap back on.

To each type of sampler, 2 ml of 1000 mg l⁻¹ MOP in dimethyl sulfoxide were added and the excess solution was removed by pumping on the sampler at a flow rate of 1.0 l min⁻¹. The DuPont (Wilmington, DE, USA) Alpha 1 constant-flow, air-sampling pump used to remove the excess solvent is capable of drawing up to 2.0 l min⁻¹ of air and was also used to obtain air samples during spray-painting (field) operations.

Description of spray-painting operations

Six different spray-painting operations (12 sampling events) were evaluated at Hill Air Force Base. Operations 41 and 42 involved painting the lower fuselage of an F-16 fighter aircraft. Operations 43 and 44 involved painting aircraft parts and under the wing of a C-130 cargo aircraft, respectively. Operation 45 involved fully painting an F-16 fighter aircraft. Operation 46 involved painting the landing gear and door area of the airplane.

All spray guns were high volume, low pressure (HVLP). Airverter, Devilbiss, Binks and Sata spray guns were used for operations 41 and 42, 43, 44, 45 and 46, respectively. In all operations, the painters used cloth coveralls and gloves and a supplied air hood.

In operations 41, 42, 44 and 45, a gray polyurethane paint formulation (Deft, Irvine, CA, USA) was used containing a 3:1 (polyenamel-to-hardener) ratio. In operations 43 and 46, sea foam green and white gloss polyurethane paint formulations (Deft) were used containing a 1:1 (polyenamel-to-hardener) ratio, respectively.

Sampling strategy

For all operations, sampling was performed by positioning a cassette sampler and an IOM sampler about 2.5 cm apart on a cart at approximately breathing zone height. For operations 41, 42 and 45, the cart was positioned about 1.8 m behind the fuselage. For operation 43, the cart was 0.6 m behind the parts. For operation 44, the cart was positioned under the aircraft wing. For operation 46, the cart was positioned 1.2 m to the right of the parts being painted. All cart positions were in the maximum overspray area.

The sampling protocols described in NIOSH Method 5521 were used throughout.¹² The isocyanate samples were collected at an air flow rate of 1.0 l min⁻¹. Sampling times ranged from 13 to 62 min.

After collection, the sponges in the samplers were immediately removed from the cassette and IOM samplers and placed in a sampling bottle containing 10 ml of 50 mg l⁻¹ MOP in acetonitrile. The sampling bottles were shipped within 2 d of sampling.

Preparation of samples

When the samples arrived in the analytical laboratory, they were prepared for analysis within 1 d. The sponges were extracted three times with 10 ml of acetonitrile and the extracts were combined and then evaporated under a gentle stream of nitrogen to a known fixed volume (2–5 ml). Each sample was separated into two equivalent fractions; one was used unchanged (non-acetylated sample) whereas to the second an additional 30 µl of acetic anhydride were added (acetylated sample).

Samplers which were not used for the collection of isocyanate were also treated in the same way as the actual samplers and served as method blanks.

Instrumentation for analysis

The extract from the sponges was analyzed using an HPLC system consisting of a Beckman (Fullerton, CA, USA) Model 110 B solvent delivery system, a Beckman Model 270A sample injector and a Beckman Model 160 ultraviolet–visible (UV) detector set at 254 nm and connected to a Hitachi (San Jose, CA, USA) Model D-2500 integrator. A BAS (Lafayette, IN, USA) electrochemical (EC) detector operated in the oxidative mode (+0.8 V *versus* Ag/AgCl) followed the UV detector. The EC cell was controlled by a BAS Model LC4B amperometric detector and the output was delivered to a Varian (Palo Alto, CA, USA) Model 4400 integrator. The column used was a Phenomenex (Torrance, CA, USA) Prodigy (100 × 4.60 mm id) C₈ PEEK column (5 µm with 150 Å pores).

The mobile phase varied between 30 + 70 and 40 + 60 acetonitrile–methanolic acetate buffer (0.6% sodium acetate in 50 + 50 methanol–water adjusted to pH 6.0 with glacial acetic acid). The mobile phase flow rate was set at 1.0 ml min⁻¹. The injection volume was 20 µl.

A Waters (Milford, MA, USA) Quanta 4000 system equipped with a Hewlett-Packard (Avondale, PA, USA) 3390A integrator was used for the CZE analysis of samples. All samples were injected using hydrostatic injection for 10 s. The capillary column had an effective separation length of 40–50 cm and an id of 75 µm. The total column length was 48–58 cm. The operating voltage was set at 20 kV. The detector wavelength was set at 185 nm. The capillary was purged with 0.5 M KOH for 3 min, then water for 3 min, then running buffer for 5 min between each run.

The running buffer varied between 0 + 100 and 50 + 50 acetonitrile–phosphate buffer [0.010 M anhydrous sodium phosphate (Na₃PO₄) in distilled water]. The pH was adjusted to

3.0 with concentrated phosphoric acid after the addition of acetonitrile.

Identification and quantification

For HPLC analysis, the peak produced by derivatized HDI monomer was identified by matching its retention time with that of HDI-MOP standards. The N-100 oligomer peaks were also identified by matching their chromatographic retention times with those of the N-100-MOP standards. The HDI-based oligomer peaks in field samples were identified by comparing them with those produced from the derivatized bulk catalyst used in the spray-painting operation. In addition, HDI-based oligomer peaks were confirmed by comparing their EC/UV response ratio with that obtained using HDI-MOP standards.

For CZE analysis, the peak produced by derivatized HDI monomer was identified by matching its migration time with those of HDI-MOP standards. The N-100 oligomer peaks were also identified by matching their migration times with those of the N-100-MOP standards. HDI monomer in field samples was identified by the method of standard additions, a sample being run with and without added HDI-MOP standard. The HDI-based oligomer peaks in field samples were identified by comparing them with those produced from the derivatized bulk catalyst used in the spray-painting operation.

For comparison of the HPLC and CZE methods, quantification of HDI monomer and HDI-based oligomers was based on calibration curves prepared with HDI-MOP and N-100-MOP standard solutions. For field studies, quantification of HDI monomer and HDI-based oligomers was based on calibration curves prepared from HDI-MOP standard solutions. All quantifications were based on the average of at least two runs.

Results and discussion

CZE method development

Effect of added organic modifier. A mixture of 40 μM HDI-MOP, 32 μmol of isocyanate groups per liter N-100-MOP and excess MOP can easily be separated using CZE, but N-100-MOP gives a very poor peak shape in an aqueous phosphate buffer (pH 3.0). By adding acetonitrile to the running buffer, the N-100-MOP peak becomes narrower with an improved peak profile. This is attributed to the fact that the acetonitrile helps to dissolve the N-100-MOP in the running buffer.

The electropherograms which illustrate the effect of added acetonitrile on the CZE separation are shown in Fig. 1. The peak for N-100-MOP becomes sharper upon adding acetonitrile up to a concentration of 40 + 60 acetonitrile-phosphate buffer. At a concentration of 50 + 50, the HDI-MOP peak begins to broaden. Concurrently, as the acetonitrile concentration in the mobile phase varies from 0 to 50%, the UV response factor for HDI-MOP and N-100-MOP double and triple, respectively. The peak area ratio of N-100-MOP to HDI-MOP increases from 56 to 105% as the mobile phase composition increases from 0 + 100 to 40 + 60 acetonitrile-phosphate buffer (see Fig. 2). The peak area ratio for a solution containing an equimolar amount of HDI and N-100 should be 1.50 if N-100 is presumed to have 3 mol NCO per mole of N-100 and HDI has 2 mol NCO per mole of HDI, and all the absorbance can be attributed to the MOP derivatizing reagent. If the $\text{N}(\text{C}=\text{O})\text{N}$ moiety between the piperazine of the MOP reagent and the hexamethylene of HDI and N-100 also absorbs, then the total absorbance will increase but the absorbance ratio will remain 1.5. The migration time (t_m) for both HDI-MOP and N-100-MOP also increases with increasing concentration of acetonitrile. This can be attributed

to the addition of organic solvent, which probably decreases the degree of protonation of the MOP-isocyanate derivatives while not affecting the degree of protonation of the more basic free MOP.

Effect of added acetic anhydride. In HPLC analysis, acetic anhydride is used to improve the analytical efficiency and to prevent excess derivatizing reagent (amine) from attaching to the silica substrate. The same problems as observed in HPLC also have been observed in CZE. If the excess of derivatizing reagent (MOP) is not converted into the amide (acetylated), then the excess MOP sticks to the capillary wall.

In a standard solution containing acetic anhydride, the migration times of HDI-MOP and N-100-MOP (5.60 and 5.85 min, respectively) differ from those in the solution without acetic anhydride (6.03 and 6.33 min, respectively), but the excess MOP peak shifts from before to after the isocyanate-MOP peaks upon addition of acetic anhydride ($t_m = 4.13$ min without added acetic anhydride and 6.47 min with added acetic anhydride).

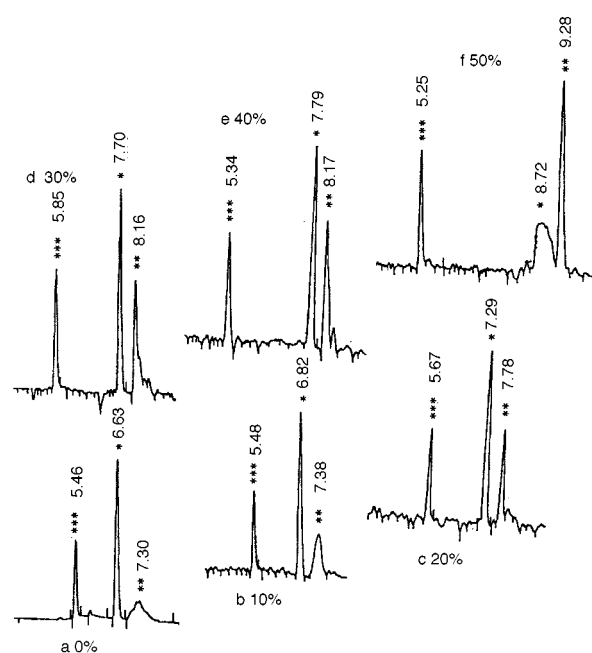


Fig. 1 Effect of acetonitrile on CZE analysis. Capillary, fused silica (50 cm \times 75 μm id); applied voltage, 20 kV; UV detector, 185 nm; running buffer, 0 + 100 to 50 + 50 acetonitrile-aqueous phosphate buffer: (a) 0 + 100; (b) 10 + 90; (c) 20 + 80; (d) 30 + 70; (e) 40 + 60; (f) 50 + 50. *, HDI monomer; **, HDI oligomer; ***, excess MOP.

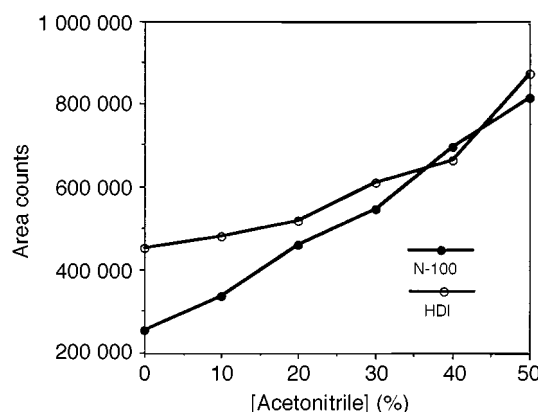


Fig. 2 Effect of acetonitrile on the CZE response of HDI and N-100. Capillary, fused silica (50 cm \times 75 μm id); applied voltage, 20 kV; UV detector, 185 nm; running buffer, 0 + 100 to 50 + 50 acetonitrile-aqueous phosphate buffer.

The average relative standard deviation (RSD) was based on five standards run in triplicate. If the migration times are compared, the average RSD for the migration time for acetylated samples is 1.8% for HDI-MOP and 1.9% for N-100-MOP. The average RSD for non-acetylated samples is 4.0% for HDI-MOP and 4.5% for N-100-MOP. The average RSD for the integrated peak area for acetylated samples is 8.1% for HDI-MOP and 14.2% for N-100-MOP. The average RSD for non-acetylated samples is 9.5% for HDI-MOP and 13.3% for N-100-MOP.

Both acetylated and non-acetylated samples have a good linear relationship between the UV response and the concentration of NCO groups. The Pearson correlation coefficient (r) values for acetylated samples ($r > 0.999$ for HDI-MOP, $r > 0.996$ for N-100-MOP) are better than those obtained for non-acetylated samples ($r > 0.993$ for HDI-MOP, $r > 0.991$ for N-100-MOP). The sensitivity (slope of the calibration curve) for acetylated samples (3051 per μM of NCO in HDI and 2746 per μM of NCO in N-100) also is better than that for non-acetylated samples (2526 per μM of NCO in HDI and 2411 per μM of NCO in N-100).

Because of the more reproducible migration times and better sensitivity after treating standards with acetic anhydride, all further CZE analyses involved samples that had been acetylated.

Comparison of HPLC with CZE

Both calibration curves obtained for HDI-MOP when using HPLC and CZE are linear ($r > 0.990$). The HDI sensitivity for CZE (3051 per μM of NCO) is about five times larger than that for HPLC (584 per μM of NCO). The HDI detection limit for CZE (0.08 mg l^{-1} ; $1.0 \mu\text{M}$ NCO) is about the same as that for HPLC (0.08 mg l^{-1} ; $1.0 \mu\text{M}$ NCO).

A comparison of calibration curves obtained for N-100-MOP when using HPLC and CZE shows a more linear relationship for CZE analysis ($r > 0.996$) than for HPLC analysis ($r > 0.987$). The N-100 sensitivity for CZE analysis (2746 per μM of NCO) is about nine times larger than that for HPLC (291 per μM of NCO). The N-100 detection limit for CZE ($5.0 \mu\text{M}$ NCO) is not as low as that for HPLC ($2.5 \mu\text{M}$ NCO).

If the slope of the N-100-MOP calibration curve is compared with that of the HDI-MOP calibration curve from HPLC analysis, the slope ratio (N-100-MOP/HDI-MOP) is 50%, which is lower than the value of 90% obtained from CZE analysis. This has important implications when trying to compare polyisocyanate results obtained from HPLC and CZE when using HDI-MOP standards. The higher response of HDI oligomer when using HDI-MOP as a standard for CZE partially explains why CZE analysis always gives higher HDI oligomer concentrations than HPLC analysis for field samples (see below).

Analysis of samples obtained during spray-painting operations

Fig. 3 illustrates (a) HPLC and (b) CZE results for a bulk catalyst used in spray-painting. In the HPLC trace, three peaks (**) are obtained from the HDI oligomer, but no HDI monomer peak (*) because of a huge excess of MOP (***). In the CZE electropherogram, both HDI monomer (*) and two oligomer (**) peaks are separated from the excess MOP peak (***). There is usually a third peak in CZE which follows the two HDI oligomer peaks, but because of its small size, it is difficult to confirm and quantify as an isocyanate.

A number of samples were acquired during spray-painting operations at Hill Air Force Base and subjected to both HPLC and CZE analyses. The samples from operation 42 were not

included in Table 1 because of a short sampling time (13 min).

Table 1 illustrates the results for HPLC and CZE analysis of HDI and HDI oligomer during spray-painting operations. In nine out of ten samples HDI oligomer data obtained from CZE analysis (column 3; $0.53\text{--}3.19 \text{ mg m}^{-3}$) are significantly higher than those obtained from HPLC analysis (column 2; $0.0\text{--}2.30 \text{ mg m}^{-3}$). The reason lies in a different N-100-MOP/HDI-MOP response ratio for CZE and HPLC. If the CZE data are adjusted by multiplying by a relative response factor of 50/90 (the response ratio of N-100-MOP/HDI-MOP from HPLC divided by the response ratio of N-100-MOP/HDI-MOP from CZE), the CZE results can be normalized for a direct comparison with the HPLC results. If a paired t -test is then used to compare HDI-based oligomer concentrations obtained using CZE and HPLC (see data pairs in columns 2 and 4), the difference between means is not significant at the 0.05 level. The results indicate that either HPLC or CZE may be used for the determination of HDI oligomer in the spray-painting environment.

HDI monomer peaks were not detected using HPLC (Table 1, column 5), but HDI monomer was detected using CZE at 185 nm with a concentration in the range $0.003\text{--}0.033 \text{ mg m}^{-3}$.

Comparing HPLC and CZE analysis, the CZE method offers better sensitivity for both HDI monomer and oligomer, shorter

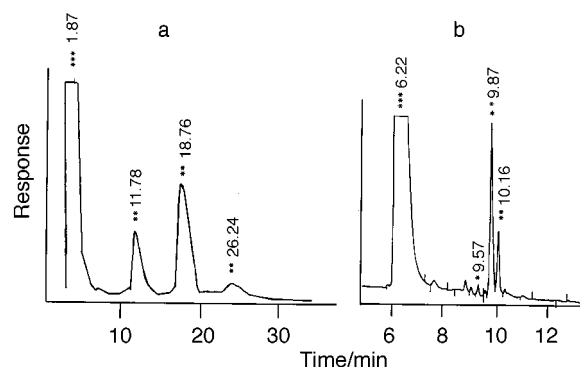


Fig. 3 Comparison of HPLC and CZE separations of a bulk catalyst. (a) HPLC. UV detector, 254 nm; column, Phenomenex ($100 \times 4.60 \text{ mm id}$) C_8 PEEK ($5 \mu\text{m}$); mobile phase, 30 + 70 acetonitrile-methanolic acetate buffer. (b) CZE. UV detector, 185 nm; capillary, fused silica ($50 \text{ cm} \times 75 \mu\text{m id}$); applied voltage, 20 kV; running buffer, 40 + 60 acetonitrile-phosphate buffer. *, HDI monomer; **, HDI oligomer; ***, excess MOP.

Table 1 Comparison of HPLC and CZE determination of isocyanates during spray-painting operations at Hill AFB

Sampler (volume) ^a	HDI oligomer/ mg m^{-3}			HDI monomer/ mg m^{-3}	
	HPLC	CZE	CZE (adj.) ^b	HPLC	CZE
41021-CAS (32 l)	1.55	1.86	1.03	< LOD ^c	0.026
41101-IOM (30 l)	1.07	1.50	0.84	< LOD	0.013
43023-CAS (23 l)	0.46	1.87	1.04	< LOD	0.031
43103-IOM (24 l)	2.30	3.19	1.79	< LOD	0.012
44024-CAS ^d (62 l)	0.41	0.67	0.37	< LOD	0.021
44104-IOM ^d (62 l)	0.82	1.80	1.00	< LOD	0.007
45025-CAS (62 l)	0.74	1.26	0.71	< LOD	0.033
45105-IOM (62 l)	0.83	1.28	0.72	< LOD	0.003
46026-CAS (31 l)	0.04	0.53	0.30	< LOD	0.023
46106-IOM (31 l)	1.49	0.69	0.39	< LOD	0.005

^a Sampler (volume) refer to the laboratory sample number followed by the acronym for the sampler (CAS = cassette, IOM = personal sampler) followed by the volume of air sampled. ^b Normalized CZE results. ^c < LOD = below limit of detection. LOD = $0.08 \mu\text{g}$ of HDI per sample for HPLC analysis and $0.08 \mu\text{g}$ of HDI per sample for CZE analysis. ^d All samples used in CZE analysis contained acetic anhydride except for 44024-CAS and 44104-IOM.

analysis time, lower buffer consumption and smaller sample requirements. However, there are a few problems in the CZE method. First, the capillary used in CZE analysis is very easily ruined by some compounds (*e.g.*, MOP) in samples so that the capillary has to be replaced every few weeks. Second, the migration time and the resolution of isocyanate peaks are very sensitive to the pH of the buffer so that it is very difficult to obtain reproducible migration times during routine analysis. This necessitates the use of the method of standard additions in order to be certain of the identity of HDI–MOP. These two disadvantages, however, are mitigated by the ability of CZE to determine both HDI monomer and HDI oligomer under the same optimum run conditions even in the presence of a huge excess of derivatizing reagent.

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