Development and Application of a Dichotomous Vapor/Aerosol Sampler for HDI-Derived Total Reactive Isocyanate Group

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A dichotomous vapor/aerosol sampler was developed for measurement of HDI (1,6-hexamethylene diisocyanate)-derived total reactive isocyanate group (TRIG). The sampler consisted of an impactor or cyclone inlet, followed by an annular diffusional denuder, and a glass-fiber filter backup. The denuder walls and backup filter were each coated with 20 mg tributylphosphate and 1 mg MAMA reagent (9-N-methylamino-methylanthracene). After collection, MAMA-derivatized isocyanates were desorbed from the sampler and determined by high-performance liquid chromatography with dual-wavelength ultraviolet absorbance and fluorescence detection. Test atmospheres of HDI vapor and of HDI/HDI-biuret aerosols were generated in the laboratory and sampled with the optimized dichotomous sampler. Vapor phase HDI was completely collected by the diffusional denuder. When a mixture of HDI-biuret and HDI (~30 ppb) was nebulized and collected with the dichotomous sampler, approximately 78% of the HDI was in the vapor phase, whereas about 22% was associated with the aerosol fraction. The dichotomous sampler was then used to measure vapor and condensed phase TRIG in a paint spray booth during application of a polyurethane paint. Measured levels of TRIG during the spraying operation averaged 391 ± 154 $\mu g/m^3$. Concentrations of HDI monomer averaged only 14 ± 6.5 $\mu g/m^3$. HDI-biuret was the largest component of TRIG found in these samples and was completely in the condensed aerosol phase. In contrast, the majority of the HDI was in the vapor phase, but significant (15–26%) amounts were measured in the aerosol fraction of the paint overspray. Thus, significant partitioning of HDI between vapor and condensed phases was demonstrated in both the laboratory and field, even when its concentration was well below the vapor saturation point.

Keywords: HDI, isocyanates, polyurethanes, spray paint, denuder, dichotomous sampling

The isocyanates form an important group of industrial chemicals used in formulating polyurethane foams, plastics, and paints. Certain isocyanate compounds such as 2,4- and 2,6-toluene-diisocyanate (TDI), 4,4′-methylene-bis-phenylisocyanate (MDI) and 1,6-hexamethylene-diisocyanate (HDI) are known to cause occupational asthma and other respiratory diseases.[1,2] However, there is increasing concern that other isocyanate compounds are formed from chemical reactions occurring when polyurethanes are manufactured or are degraded by hot processes, and that these isocyanates may

also be capable of causing occupational diseases. These isocyanate-containing compounds, along with the parent isocyanate monomers, oligomers and prepolymers comprise total reactive isocyanate group (TRIG). Although the health effects of exposure to monomeric diisocyanate are well known, and current research efforts are aimed at refining the dose-response relationship, less information has been developed concerning the toxicology of TRIG. Animal models have indicated HDI-biuret to be a potent pulmonary irritant and have suggested an allowable exposure level of about 0.5 mg/m³.[3] There are many case

reports in the literature linking exposure to polyisocyanates—primarily from spray painting—to various pulmonary diseases, including asthma[4,5] and hypersensitivity pneumonitis.[6,7] In contrast, there are currently no population-based studies in the literature directly concerning chronic TRIG exposure-related health effects.

Legal standards and exposure guidelines exist for the widely used TDI, MDI, and HDI diisocyanate monomers. However, other than in the state of Oregon, which has an exposure standard for HDI-based polyisocyanates, no exposure guidelines for these other isocyanate compounds currently apply in the United States. Internationally, the United Kingdom has developed an exposure standard for total reactive isocyanate group under the assumption that the isocyanate functional group is inherently responsible for observed health problems associated with exposure, regardless of the organic moiety to which the isocyanate group is attached. Thus, the allowable exposure level is 20 μg TRIG per m³ of air, which is simply based on an extrapolation of the equivalent TRIG level for 2,4-TDI, the standard for TDI being 40 μg/m³, and there being 0.48 μg TRIG per μg TDI.

To evaluate exposures to these isocyanate-containing materials, reliable techniques for their collection and measurement in the workplace are needed. Recently, this laboratory has demonstrated a new analytical approach to the measurement of TRIG that allows for its identification and quantitation even when its exact chemical identity is uncertain.[8,9] The technique uses 9-N-methyl-aminomethyl-anthracene (MAMA) reagent to form urea derivatives with all available isocyanate groups. The resulting ureas contain the anthracenyl group, which is highly fluorescent and chromophoric in the ultraviolet (UV). Thus, high-performance liquid chromatography with UV and fluorescence detection for the anthracenyl group can be used to specifically identify and quantitate these ureas. This new technique was shown to be superior to other currently used methods for TRIG in terms of specificity, accuracy, ease of use, and reliability.

The technique was also adapted to a new sampling device that enables separate measurement of TRIG in the vapor phase and in the aerosol or condensed particle phase.[10–12] The dichotomous sampler for TRIG aerosol and vapor consisted of an impactor or cyclone inlet for collection of nonrespirable aerosols followed by an annular diffusional denuder tube for collection of vapor. This is then backed up by a treated filter or impinger for collection of respirable aerosol.

The identification and measurement of TRIG in workplace atmospheres is an important first step in examining this potential occupational health hazard. Furthermore, knowledge of how TRIG partitions between vapor and particulate phases is important in understanding where the material deposits in the body when it is inhaled, and is also useful in designing appropriate control technologies, such as air filtration systems, for minimization of worker exposure. In this work, the authors have combined the MAMA reagent and the annular denuder sampler into a technique for measuring HDI-derived TRIG and speciating it into vapor and aerosol fractions. The development of the technique and its application for measurement of HDI-derived TRIG in the laboratory and field are described.

METHODS AND MATERIALS

The oligomeric form of HDI used in the study was HDI-biuret, a trimer of HDI. The source material was Desmodur N100 (Bayer Chemical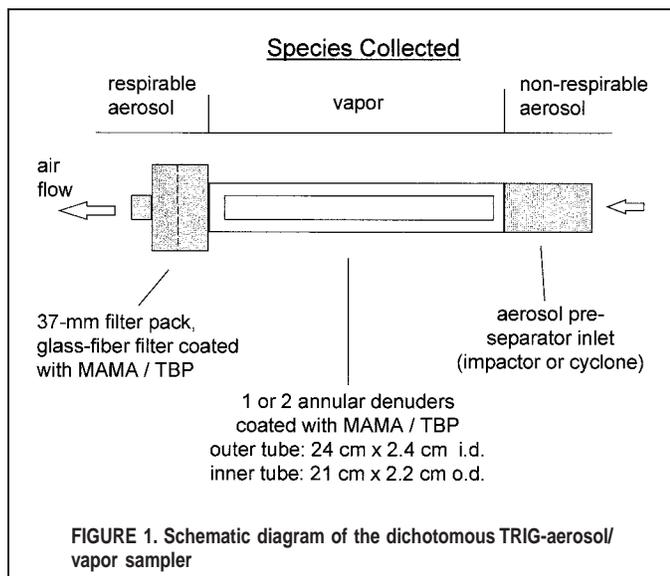 Co., Pittsburgh, Pa.). The bulk test material was assayed for TRIG content using the MAMA technique as follows: a known mass of Desmodur N100 (0.1–0.3 g) was weighed out and dissolved in dimethylsulfoxide. The expected number of moles of isocyanate present was calculated based on the results of a reference assay done by titration with di-n-butylamine and hydrochloric acid.[13] The sample was then reacted with a three- to five-fold excess of MAMA, based on a stoichiometric reaction of one mole of MAMA with one mole of isocyanate group. The MAMA reagent was dissolved in the same solvent as the isocyanate-containing material prior to its addition. After allowing sufficient time for reaction, the sample was then analyzed by high-performance liquid chromatography (HPLC).

Chromatographic analysis of the MAMA-derivatized samples (bulk test material and air samples) and standards was performed with detection by fluorescence using a Shimadzu Model RF551 fluorometric detector with excitation at 245 nm and emission at 414 nm, and by ultraviolet absorption at two wavelengths using a Perkin Elmer Model LC90 UV detector set at a wavelength of 245 nm and a Waters Model 450 UV detector set at a wavelength of 370 nm. Sample injection volumes were defined by a 20-μL sample loop. Samples were analyzed on a Supelcosil LC-8-DB octyl bonded phase column, 5 μm particle size (Supelco, Belafonte, Pa.), 4.6 mm i.d. by 5 cm long. The mobile phase consisted of a mixture of 60% acetonitrile and 40% aqueous triethylammonium phosphate buffer (3% triethylamine in water, adjusted to pH 3.0 with phosphoric acid).

Chromatograms were screened for the presence of TRIG-derived peaks by comparison with the HDI parent monomer standard. The criteria for classification of a peak as being a TRIG-containing compound was a detector response ratio for UV absorbance at 245 nm to that at 370 nm within ±20% of that for the monomer standard. The 20% criteria was derived as an approximation of the 95% confidence interval of the overall mean detector response ratio observed for 11 different isocyanate monomers previously screened with this technique.[8] Further confirmation of the identity of an unknown TRIG-containing compound was provided by examination of its fluorescence response. In general, the fluorescence response of the identified TRIG compounds was of the same order of magnitude as the corresponding HDI monomer standards, although there appeared to be a general trend of decreasing fluorescence with increasing chromatographic retention time. After identification of a TRIG compound, the amount of isocyanate present was determined in comparison with the response of the HDI parent monomer standard. This was done for each of the UV absorbance detectors independently. Calibration of detector response for quantitation of TRIG in these compounds used conversion factors based on two moles TRIG/mole of diisocyanate monomer standard; i.e., for HDI, 0.138 μg TRIG/μg HDI-MAMA urea.

Dichotomous Sampler

The dichotomous sampler was obtained from University Research Glassware (Model 2000, URG, Carrboro, N.C.). The device consisted of an annular denuder in series with a size selective aerosol preseparator (cyclone or impactor inlet) and an aerosol filter or impinger backup (Figure 1). All components were made of borosilicate glass, Teflon®, or stainless steel. The inlet to the denuder used either of two aerosol preseparators: an 11-mm diameter glass tube that acted as an elutriator, followed by an acceleration jet and 1.1-cm diameter porous stainless steel impaction plate (D_{50} = 2.5 μm at a sampling flow rate of 10 L/min), or an aluminum cyclone with D_{50} = 2.5 μm at a flow rate of 2.8 L/min. The preseparator

Species Collected

respirable aerosol — vapor — non-respirable aerosol

air flow →

37-mm filter pack, glass-fiber filter coated with MAMA / TBP

1 or 2 annular denuders coated with MAMA / TBP
outer tube: 24 cm x 2.4 cm i.d.
inner tube: 21 cm x 2.2 cm o.d.

aerosol pre-separator inlet (impactor or cyclone)

FIGURE 1. Schematic diagram of the dichotomous TRIG-aerosol/vapor sampler

rate of 10 L/min, the collection efficiency of a single denuder tube for HDI vapor is predicted to be 95.3% using Possanzini's algorithm,[14] assuming a diffusion coefficient of 0.054 cm²/sec for HDI and perfect absorption by the denuder walls. At a flow rate of 1 L/min, the predicted efficiency rises to a value of 100%.

Testing of the Dichotomous Sampler with MAMA Reagent

A series of laboratory investigations were carried out to adapt the MAMA reagent system to use in the dichotomous sampler and to optimize its performance for speciating vapor and aerosol forms of HDI-based TRIG. Initial work was done with HDI monomer vapor. For collection and speciation of HDI vapor by the dichotomous sampler, the following factors were evaluated: sampler flow rate (1, 2.8, and 10 L/min), the amount of MAMA reagent coated on the dichotomous sampler stages (100 μg or 1 mg), incorporation of a nonvolatile liquid in the coating (tributylphosphate), and treatment of the impactor stage with MAMA reagent. These investigations are outlined in Table I.

Experiments 1–3 were carried out using test atmospheres produced in a laminar flow test chamber.[15,16] Nitrogen was bubbled through liquid HDI contained in a fritted glass bubbler (Ace Glass Cat. No. 7430). The HDI-saturated nitrogen was then passed through a glass-fiber filter prior to being injected into the chamber. The concentration of HDI vapor during these tests ranged from 67 to 302 ppb. In each run two denuder sections were used in series. They were coated with 100 μg MAMA reagent by adding the appropriate amount of MAMA in hexane to the denuder, and evaporating the hexane under a flow of nitrogen. The backup filters in Experiments 1 and 2 were coated with MAMA by dipping in the MAMA/hexane solution and evaporating off the hexane

was followed by the first annular denuder section, consisting of inner and outer glass cylinders with an annular spacing of 0.1 cm in between. The outer diameter of the denuder tube was 2.6 cm, and the length was 24 cm. Other sections of denuder tube were placed in series as desired, using specially designed couplings that sealed with Teflon-coated O-rings. The final stage of the sampler was typically a 37-mm Teflon filter holder containing a treated glass fiber filter. For certain experimental runs, an impinger containing MAMA in acetonitrile or dimethylsulfoxide was used as the final stage in the dichotomous sampler. At a sampling flow

TABLE I. Initial Evaluations of MAMA Dichotomous Sampler for HDI Vapor

| Experiment Series No. | Experimental Conditions | | | | Dichotomous Sampler Component | Distribution of Isocyanate (% of Total, Mean ± SD) |
	Flow Rate	Coating	Backup Type	Impactor Coated		
1 n = 5	10 L/min	100 μg MAMA	treated filter	N	filter denuder 2 denuder 1 impactor	34 ± 22 23 ± 16 43 ± 15 0.6 ± 1.1
2 n = 5	1 L/min	100 μg MAMA	treated filter	N	filter denuder 2 denuder 1 impactor	58 ± 42 1.8 ± 3.6 41 ± 37 0.7 ± 1.1
3 n = 5	2.8 L/min	100 μg MAMA	impinger	N	impinger denuder 2 denuder 1 impactor	4.5 ± 5.0 31 ± 12 64 ± 8.1 0 ± 0
4 n = 5	2.8 L/min	100 μg MAMA and 20 mg TBP	impinger	N	impinger denuder 2 denuder 1 impactor	0.7 ± 1.5 14 ± 10 85 ± 11 0.1 ± 0.2
5 n = 5	2.8 L/min	1 mg MAMA	impinger	Y	impinger denuder 2 denuder 1 impactor	0.7 ± 1.6 5.2 ± 4.9 70 ± 7.6 24 ± 7.5
6 n = 5	2.8 L/min	1 mg MAMA and 20 mg TBP	impinger	Y	impinger denuder 2 denuder 1 impactor	0 ± 0 2.9 ± 4.3 81 ± 11 16 ± 6.8

FIGURE 2. Schematic diagram of the isocyanate aerosol test chamber
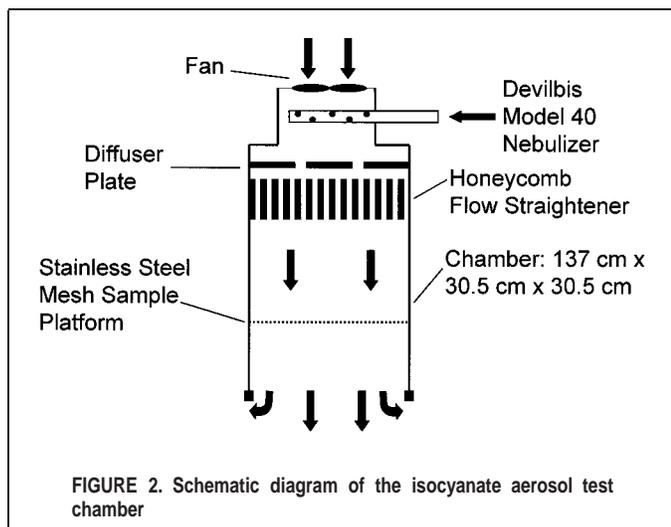
under a nitrogen flow. Using this procedure, the filters were coated with approximately 200 μg of MAMA. In Experiment 3 the backup impinger contained 10 mL of a solution of 100 μg/mL MAMA in acetonitrile. After sample collection each component of the dichotomous sampler was desorbed/treated and analyzed by HPLC: The impactor plates were removed immediately after sampling and placed into 1 mL of the MAMA/acetonitrile solution; the denuders were desorbed with 2.0 mL acetonitrile; the treated filters were desorbed in 1.0 mL of acetonitrile and passed through a syringe filter prior to analysis; and the impinger sample solutions were brought back to volume with acetonitrile and analyzed directly. For each sampling run in this initial series of experiments, a reference sample was collected using the nitro reagent-coated filter technique followed by HPLC analysis. [17]

Experiments 4 through 6 were conducted with a bench-top system for generating test atmospheres, and HDI vapor was generated using a silicone rubber permeation tube.[18] Dry air was passed over the permeation tube, which was held at a constant temperature, and subsequently diluted with room air, resulting in test atmospheres containing 75 ± 10 ppb of HDI. In these experiments the sampler flow was held constant at 2.8 L/min. The denuders were prepared for sampling in the following ways: coated with 100 μg MAMA and 20 mg tributylphosphate (TBP); coated with 1 mg MAMA; coated with 1 mg MAMA and 20 mg TBP. TBP is a nonvolatile, viscous liquid that was added to improve the collection of HDI vapor. TBP is transparent under the HPLC detection conditions used for analysis of MAMA-derivatized isocyanate samples and thus does not interfere with the method. Also, the impactor plate was coated with derivatizing agent in Experiments 5 and 6 for comparison with collection by the uncoated plate.

Dichotomous Sampling of Oligomeric Isocyanate Mixtures

Evaluation of the dichotomous sampler for measurement and speciation of oligomeric isocyanate mixtures was performed using an aerosol test chamber. A schematic of the chamber is shown in Figure 2. The chamber is a laminar flow cabinet that operates under positive pressure by dilution air forced into the top of the unit by a fan. The cross section of the chamber is 1 foot square. The fan moves air through the chamber at approximately 100 ft³/min, resulting in an average flow velocity of about 100 ft/min. Aerosol was generated using a Devilbiss Model 40 glass nebulizer. The aerosol and dilution air were mixed by passing through a

series of perforated plate diffusers. The aerosol atmosphere then passed through a honeycomb flow staightener before entering the sampling zone of the chamber. The chamber was placed in a walk-in laboratory fume hood during use.

Test atmospheres of Desmodur N100 aerosol were generated by nebulizing a solution of 1% Desmodur N100 in dimethylsulfoxide (DMSO) with the Devilbiss Model 40 nebulizer. The nebulizer was operated at a flow rate of 14 L/min using compressed air. Initial work with the dichotomous sampler used the impactor inlet and the device was evaluated at sampling flow rates of 1 L/min, 2.8 L/min, and 10 L/min. At 10 L/min the D_{50} of the impactor is 2.5 μm, whereas at 1 L/min it is estimated to be 4.8 μm. During these initial evaluations the denuders were coated with 100 μg MAMA reagent and the impactor plates were left uncoated but were desorbed with MAMA solution immediately after sample collection.

To extend the application of the dichotomous sampler for very high loadings of aerosol such as might occur in sampling paint overspray atmospheres, a cyclone inlet was investigated as a replacement for the impactor. The cyclone inlet (URG, Carrboro, N.C.) was designed with a D_{50} of 2.5 μm at a flow rate of 3 L/min. The dichotomous sampler with cyclone inlet was evaluated using the aerosol test chamber as described above. In these tests atmospheres were generated by nebulizing a solution of 1% Desmodur N100, 0.02% HDI in dimethylsulfoxide. HDI monomer was added to the mixture to increase its concentration in the test atmosphere, to allow a more accurate assessment of its collection on the various stages of the dichotomous sampler, and to aid in evaluating the partitioning of HDI between vapor and condensed phases. The denuders in this work were coated with 1 mg MAMA and 20 mg TBP. The dichotomous samplers were operated at a flow rate of 2.8 L/min. Immediately after sampling, the cyclones were washed with a MAMA solution for measurement of collected isocyanate.

Samples from these aerosol test atmospheres were also collected for particle size distribution analysis. A four-stage virtual impactor (Cascade Centripeter: BGI Inc., Waltham, Mass.) was placed in the chamber and operated simultaneously with the dichotomous samplers. The stages of the impactor were glass-fiber filters coated with the MAMA/TBP reagent in the same fashion as the backup filter of the dichotomous sampler. After collection, the impactor filters were prepared and analyzed by HPLC for collected TRIG in the same manner as previously described for the dichotomous samplers.

Field Sampling in a Working Paint Spray Booth

Field testing of the dichotomous sampler was conducted in a paint spray booth at a military facility that was being used to spray-paint vehicles with an HDI-based polyurethane paint. Sampling was conducted during the spray painting of a four-wheeled ammunition carrier. The painting was done in a 24 ft deep, 14 ft wide, and 13 ft high paint booth. The back wall of the booth was a filter plenum through which air was being exhausted at 69,000 ft³/min. A mixing/cleanup station was positioned inside the booth along one of the side walls. The spray painter was equipped with a Tyvek® supplied-air painting hood and Tyvek overalls during all mixing, painting, and cleanup operations. The vehicle was painted with Deft Green 24052 polyurethane (Deft Chemical Coatings, Irvine, Calif.). This is a two-component polyurethane paint based on HDI. The isocyanate catalyst component is a solution of 0.15% HDI, 29.8% HDI-biuret in a mixture of toluene, xylene, 2-butanone, and ethoxyethyl acetate. The base component

TABLE II. Comparison of Dichotomous Sampler and Nitro Reagent Filter Sampler for Collection and Measurement of HDI Vapor

Dichotomous Samplers (ppb HDI)	Nitro Reagent Filter (ppb HDI)
59/90	67
126/138	106
158/176	178
184/174	182
360/296	302

Note: Regression analysis: D.S. = 1.03 N.R.F. + 3.4 ppb, r = 0.965.

is a proprietary mixture of polyol, lead chromate, 2-butanone, ethoxyethyl acetate, and ethyl acetate.

Separate samples were collected during the mixing, painting, and cleanup phases of the process. Samples collected during paint mixing were stationed adjacent to and down wind from the mixing counter. During painting, samples were stationed directly in front of the filter plenum. Samples were positioned in both locations during the cleanup activity. In all cases the dichotomous samplers were placed on tripods with the sampler inlets positioned about 3.5 to 4 ft above the floor. Dichotomous samplers with uncoated impactor inlets and with cyclone inlets were used. Because of the large loading of aerosol expected, only samplers with cyclone inlets were used during the actual spraying of paint. Samplers with impactor inlets were used during mixing and cleanup. In all cases one section of denuder tube was used that was coated with 1 mg MAMA and 20 mg TBP. Backups in all cases were glass fiber filters treated with the MAMA/TBP coating solution. All samples were collected at a flow rate of 2.8 L/min. Immediately after sample collection, the impactor plate or cyclone was removed from the sampler and desorbed with a solution of MAMA reagent in dioxane to stabilize any collected TRIG.

RESULTS

The results of the correlation of the dichotomous sampler with MAMA reagent to the nitro reagent filter reference technique for HDI vapor are shown in Table II. In these experiments each nitro reagent filter sample was paired with two dichotomous samplers. Overall, the concentrations of HDI as determined by the dichotomous samplers with HPLC analysis of the MAMA derivatives correlated very well with those determined by the nitro reagent reference technique. Linear regression of the results (dichotomous sampler = dependent variable; nitro reagent sampler = independent variable) yielded a slope of 1.03, near unity, and an intercept of 3.4 ppb. In sampling the HDI-vapor test atmospheres (Experiments 1–3, Table I), insignificant amounts of HDI were found on the uncoated impactor plate. However, penetration of HDI past the denuders and onto the backup filter or impinger was significant, ranging up to 58% of the total. In addition, relatively large amounts of HDI penetrated past the first denuder to be partially collected by the second denuder in series. There was no clear effect of flow rate on the collection efficiencies of the sampler components. It is likely that the expected relationship of increased efficiency with decreased flow was being obscured by the large variability and relatively low efficiency observed in the denuder data. Review of these results suggested that modifications to the sampler design were needed to improve its performance in separating vapor phase HDI, which should be distributed only on the denuder sections, from aerosolized HDI.

The collection efficiency of the denuders was improved both by inclusion of TBP and by increasing the amount of MAMA reagent (Experiments 4–6, Table I). It is apparent that a coating of 100 μg MAMA alone is inadequate for efficient collection of HDI vapor. However, a coating of 1 mg MAMA without TBP appeared satisfactory. A further slight improvement in collection was noted with the inclusion of tributylphosphate in the 1 mg MAMA coating. A dramatic improvement in collection was noted when TBP was added to the 100 μg MAMA coating.

Significant collection of HDI vapor was seen when the impactor stage also was coated with reagent. Collection of vapor phase isocyanate on the impactor negates using the dichotomous sampler to speciate HDI into vapor and aerosol phases. Overall, these initial experiments indicated that the dichotomous sampler's denuder sections should be coated with 1 mg MAMA and 20 mg TBP, whereas the impactor plate should be left uncoated. In these conditions the impactor plate would have to be desorbed with a MAMA solution as soon after sample collection as feasible.

Desmodur N100 is primarily HDI-biuret, a trimer of HDI. The material contains a small amount of HDI monomer, which may reach a maximum of about 1.6% after long-term storage. Results of chromatographic analysis of bulk samples of Desmodur N100 are shown in Table III and Figure 3. In the chromatogram four peaks were identified as having contained isocyanate. Peak 1

TABLE III. MAMA Assay of TRIG Content of Desmodur N100

Material	Peak No.[A]	Detector Response Ratio (245 nm: 370 nm)	Weight % TRIG		
			MAMA (245 nm)	MAMA (370 nm)	Reference Assay[B]
HDI monomer standard	1	8.3 ± 2.4%	—	—	—
Desmodur	1	8.7 ± 8.0%	0.7 ± 10.2%	0.7 ± 3.0%	—
N100	2	8.9 ± 3.4%	0.7 ± 1.0%	0.7 ± 2.5%	—
Sample	3	8.4 ± 0%	11.5 ± 2.5%	11.3 ± 2.4%	—
	4	9.3 ± 3.2%	1.8 ± 2.4%	1.6 ± 2.7%	—
	5	15.5 ± 5.0%	0	0	—
Sample total		—	14.7 ± 2.5%	14.3 ± 4.4%	14.0 ± 10.0%

Note: All values are mean ± coefficient of variation.
[A]Numbers correspond to marked peaks in Figure 3.
[B]Reference assay by titration with di-n-butylamine/HCL.[(13)]

FIGURE 3. Chromatogram of a MAMA-derivatized sample of Desmodur N100 containing 98.7 micromoles TRIG per L. Numbered peaks correspond to those in Table III.
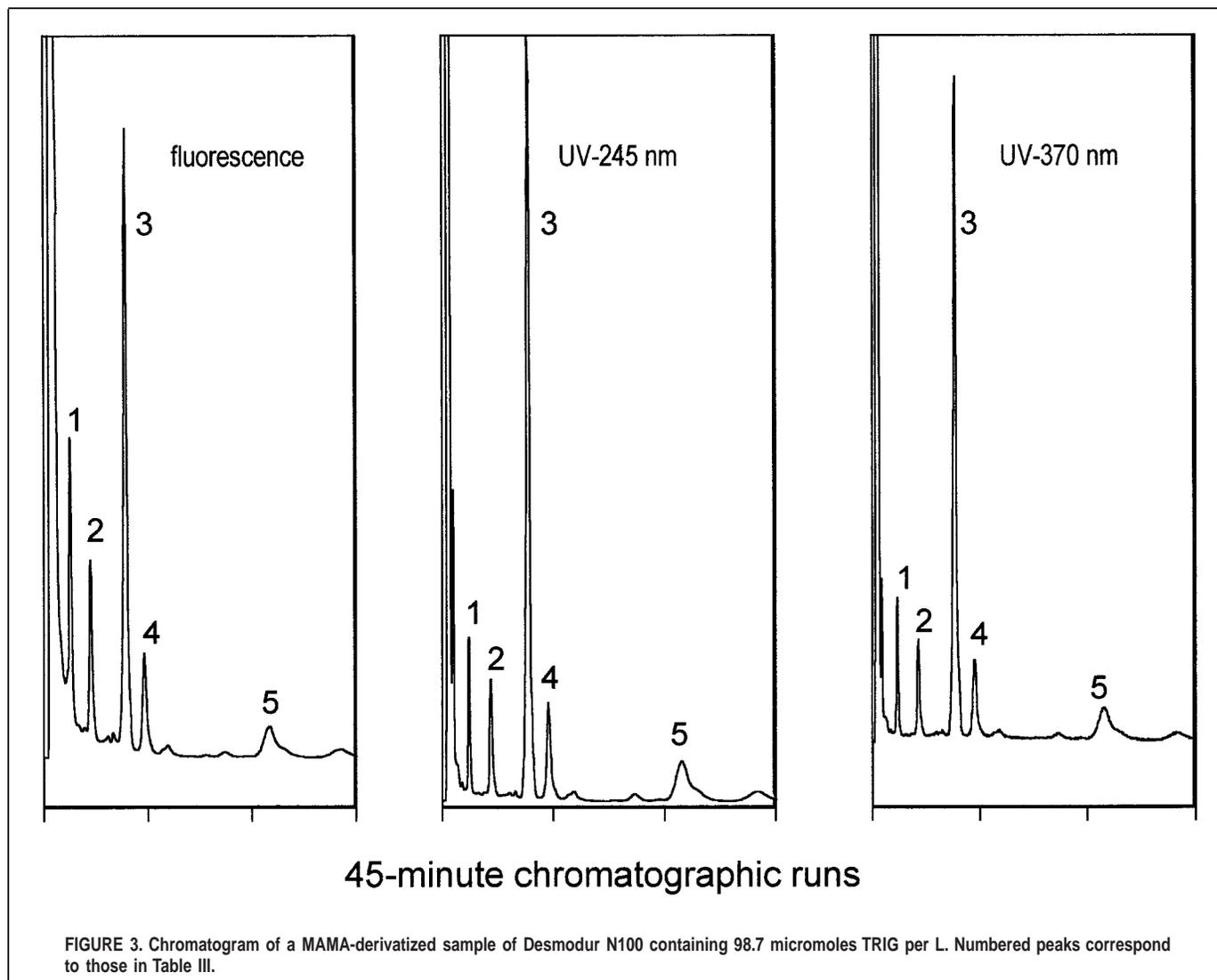
TABLE IV. Laboratory Evaluation of MAMA Dichotomous Sampler for Aerosolized Desmodur N100

Dichotomous Sampler Flow Rate	Dichotomous Sampler Component	% of HDI Collected (Mean ± SD)	% of TRIG[A] Collected (Mean ± SD)
1 L/min (n = 4)	backup filter	21.6 ± 4.3	51.6 ± 18.1
	denuder	57.5 ± 11.0	ND
	impactor	20.8 ± 13.2	48.4 ± 18.1
2.8 L/min (n = 8)	backup filter	ND	55.4 ± 12.7
	denuder	ND	ND
	impactor	ND	44.6 ± 12.7
10 L/min (n = 4)	backup filter	21.9 ± 16.3	15.7 ± 25.2
	denuder	64.0 ± 9.6	ND
	impactor	14.2 ± 21.3	84.3 ± 25.2

Note: Dichotomous sampler consists of uncoated impactor inlet, one section of annular denuder coated with 1 mg MAMA and 20 mg TBP, and backup glass-fiber filter coated with 1 mg MAMA and 20 mg TBP. ND = not detected, minimum detectable concentrations for 30-min samples = 3.3 $\mu g/m^3$, 1.2 $\mu g/m^3$, and 0.3 $\mu g/m^3$ for sample flow rates of 1, 2.8, and 10 L/min, respectively.
[A]TRIG calculated without HDI monomer.

was identified as HDI monomer and accounted for 0.7% of the total TRIG in this sample. Peak 3 was presumed to be HDI-biuret since it was clearly the largest component of the sample and accounted for 81% of the TRIG in these samples. Peaks 2 and 4 were TRIG-containing compounds of unknown structure, which were presumably other oligomeric forms of HDI. Peak 5 in the chromatogram was not considered to have contained isocyanate since its detector response ratio was 15.5 (187% of the HDI-monomer standard), which was outside of the selection criteria. The detector response ratios of the four TRIG compounds identified in these samples ranged from 8.4 to 9.3, equivalent to a range of 101 to 112% of that of the HDI-monomer standard, which had an average detector response ratio of 8.3. In comparison with the reference titration assay for isocyanate group, chromatographic analysis of the Desmodur N100 sample after treatment with MAMA yielded average recoveries of 105 and 102% for quantitation by UV absorbance at 245 nm and 370 nm, respectively.

The initial evaluations of the dichotomous sampler for collection of aerosolized Desmodur N100, as shown in Table IV, clearly illustrated the separation of HDI-biuret, which should be found essentially only in the condensed phase, from the semivolatile HDI monomer. No HDI-biuret was found on any denuder sections in

TABLE V. Laboratory Evaluation of Optimized Dichotomous Sampler with Cyclone Inlet for Aerosolized Desmodur N100 Spiked with HDI Monomer

Dichotomous Sampler Component (n = 6)	% of HDI Collected (Mean ± SD)	% of TRIG[A] Collected (Mean ± SD)
Cyclone	13.5 ± 2.1	26.7 ± 6.9
Diffusional denuder	78.3 ± 7.6	ND
Backup filter	8.3 ± 6.3	73.3 ± 15.2

Note: Dichotomous sampler consists of uncoated cyclone inlet, one section of annular denuder coated with 1 mg MAMA and 20 mg TBP, and backup glass-fiber filter coated with 1 mg MAMA and 20 mg TBP. Dichotomous sampler flow = 2.8 L/min. ND = not detected, minimum detectable concentrations = 1.0 µg/m³ for average sample volume of 116 L.
[A]TRIG calculated without HDI monomer.

these tests. The amount of HDI-biuret collected by the impactor inlet increased by almost a factor of two in going from a flow rate of 1 or 2.8 L/min to 10 L/min, reflecting the increased collection efficiency and decreased D_{50} of the impactor for higher flow rates. On average, the aerosol fraction of TRIG in these experiments exhibited a mass median aerodynamic diameter of 0.85 µm with a geometric standard deviation of 1.8, as determined by analysis of the Cascade Centripeter. The small aerosol size generated in these experiments was particularly useful for evaluating the performance of the denuder for separation of vapor and respirable aerosol. Nonrespirable aerosol, which may comprise a major part of certain industrial atmospheres such as paint overspray, is removed from the sample flow stream by the device's impactor or cyclone preseparator.

Interestingly, the HDI monomer was distributed over all three collection stages of the dichotomous sampler, although most was found on the denuder sections, which should trap only vapor phase HDI. The amount of HDI found in the backup may not be accurately reflective of the amount associated with respirable aerosols because of the use of only 100 µg MAMA on the denuders in this early work. As previously noted, poorer collection efficiency for the denuders was found with a lower loading of MAMA reagent on the denuders. Nonetheless, the impactor plates were uncoated in these experiments and they collected a significant amount of HDI monomer, indicating that substantial amounts of the material had partitioned between the vapor and aerosol phases.

For the test atmospheres of Desmodur N100 spiked with HDI monomer, the concentrations of HDI and TRIG averaged 203 µg/m³ (30 ppb) and 305 µg/m³, respectively, with the latter reported as isocyanate group and not including HDI monomer. In these tests no HDI-biuret or other oligomers of HDI were found on the denuder sections optimized with 1 mg of MAMA and 20 mg of TBP (Table V), indicating that these materials were completely in the condensed phase. In line with previous results, HDI monomer was distributed across the stages of the dichotomous sampler with approximately 78% of the material being found on the denuders (vapor phase) and 22% on the cyclone and backup filter (aerosol phase). This supports the theory that under the conditions of spray aerosolization, HDI tends to partition between vapor and condensed phases, even when the vapor concentration is about three orders of magnitude lower than its saturated vapor pressure (equivalent to approximately 3×10^4 ppb at 25°C).[19]

A representative chromatogram from a cyclone sample collected in the paint spray booth is shown in Figure 4. A single major peak corresponding to HDI-biuret is evident at a retention time
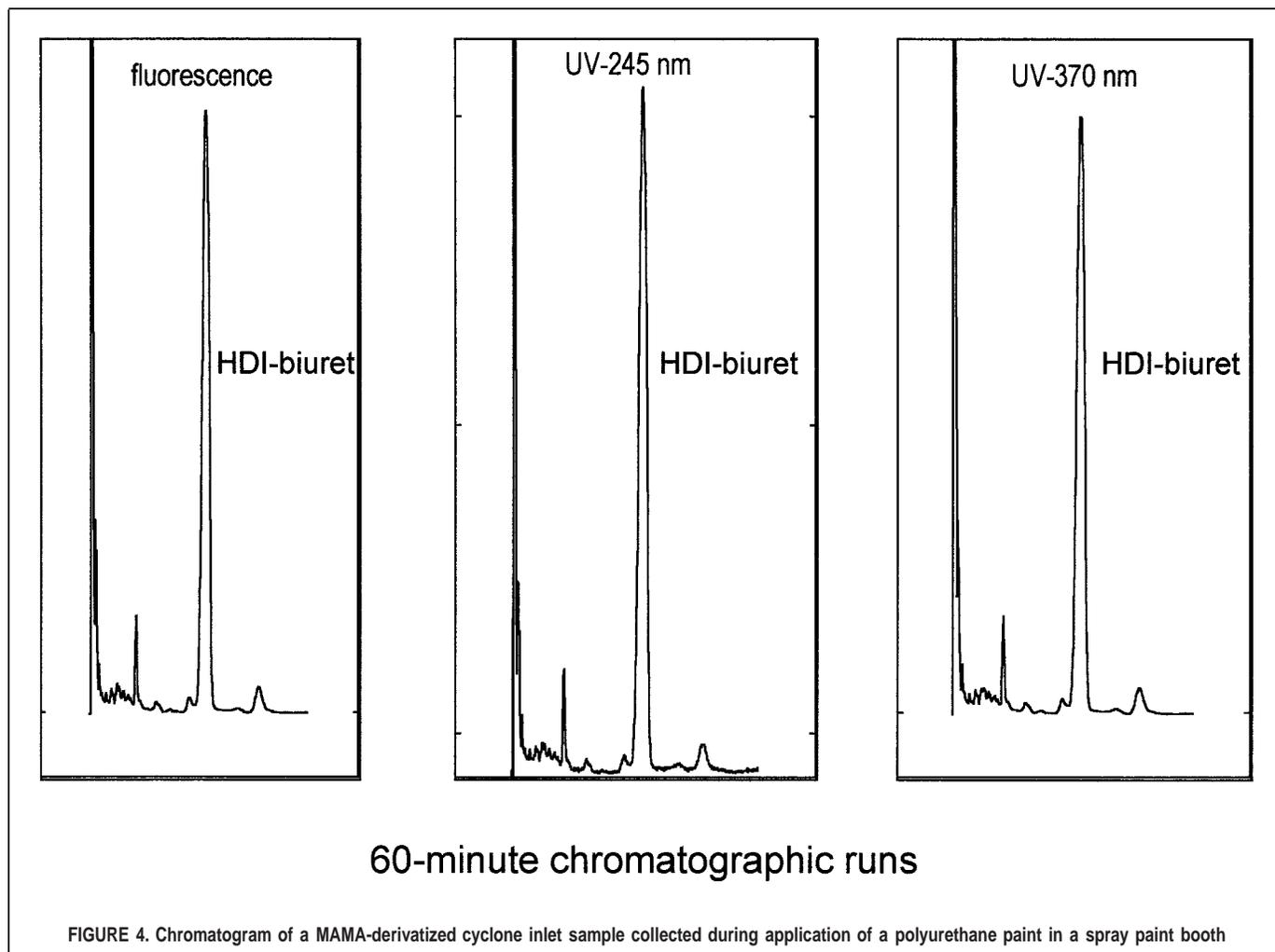
of approximately 36 min. A second smaller peak representing about 4% of the TRIG content of the sample is evident at about 14 min. A trace of HDI monomer is seen at a retention time of 10.5 min. Seven other trace-level peaks were identified in this chromatogram as having contained TRIG using the selection criteria previously described for the analysis of HDI-based TRIG samples. By far, the largest isocyanate-containing component of these samples was the HDI-biuret trimer. This compound was completely distributed in the cyclone/impactor precollector and on the back-up filter, indicating its presence exclusively as an aerosol in this workplace atmosphere.

The results from sampling during various stages of the painting process are presented in Table VI. No isocyanate was detected during the mixing operations. During painting, very high concentrations of TRIG were measured, ranging from 199 to 551 µg/m³. Again, most of this material was identified as HDI-biuret during chromatographic analysis and it was present only in the aerosol fractions of the samples. Small amounts of HDI monomer ranging from 7 to 17 µg/m³ (1 to 2.5 ppb) were measured during the painting operation. In one pair of samples, there was evidence that HDI had partitioned between vapor and aerosol phases, with 15 to 26% of the measured HDI being found in the cyclone and backup filter. These results are quite consistent with the partitioning behavior observed in the laboratory test atmospheres of Desmodur N100 and HDI. In the other sample pair from spray painting, HDI was found in small amounts on the denuder but could not be detected in the cyclone or backup filter. In contrast, all of the non-HDI TRIG was collected on the cyclone and backup filter, indicating complete separation of these compounds into the aerosol fraction of the paint overspray. During the cleanup operation only small amounts of HDI were measured and these were completely in the vapor phase (on the denuder). No other forms of TRIG were detected during cleanup. These latter results are consistent with the off-gassing of HDI vapor from the freshly painted surfaces of the workpiece.

DISCUSSION

The vapor/aerosol partitioning of isocyanate compounds arises from two sources: (1) the wide range in vapor pressures of the compounds and (2) their relatively high degree of surface affinity. The oligomeric isocyanates (e.g., HDI-biuret) are essentially nonvolatile and will exist only as mechanically generated aerosols in the atmosphere. In contrast, the isocyanate monomers have significant vapor pressures and may exist either as vapor or mixtures of vapor and aerosol, depending on concentration. For example, at 25°C, monomeric MDI has a vapor pressure equivalent to an airborne concentration of 9 ppb.[20] This is less than half the Occupational Safety and Health Administration permissible exposure limit (PEL; 20 ppb); thus, occupational exposures to MDI are commonly to a mixture of the vapor and particulate phases, depending on temperature. In previous work, the authors have used the dichotomous sampler with nitro reagent to demonstrate partitioning of homogeneous atmospheres of MDI into vapor and condensed phases.[10]

In contrast to MDI, the vapor pressures of TDI and HDI at 25°C are equal to concentrations of about 40 and 30 ppm, respectively.[19] These levels are greater than 1000 times the PEL (or threshold limit value)/short-term exposure limit of 5 ppb/20 ppb. Thus, for TDI and HDI, occupational exposures at or near the allowable levels would be expected to be primarily to the vapors of these compounds under normal circumstances. On the

FIGURE 4. Chromatogram of a MAMA-derivatized cyclone inlet sample collected during application of a polyurethane paint in a spray paint booth

other hand, although its vapor pressure is large relative to the exposure standard, TDI has been recognized as having affinity for surfaces; for example, several studies on the kinetics of hydrolysis of TDI have shown that the reaction with water occurs primarily

TABLE VI. Results of Dichotomous Sampling for Aerosols and Vapor of HDI and TRIG during Application of Polyurethane Paint in a Working Spray Booth

Activity	Concentration in Vapor Fraction (μg/m³)		Concentration in Aerosol Fraction (μg/m³)	
	HDI	TRIG[A]	HDI	TRIG[A]
Mixing	<5	<5	<5	<5
Mixing	<5	<5	<5	<5
Painting	17	<0.7	3	551
Painting	14	<0.7	5	461
Painting	7	<0.7	<0.7	199
Painting	10	<0.7	<0.7	343
Cleanup/drying	2	<1.5	<1.5	<1.5
Cleanup/drying	6	<1.5	<1.5	<1.5
Cleanup/drying	<2.7	<2.7	<2.7	<2.7
Cleanup/drying	<2.7	<2.7	<2.7	<2.7

Note: < values based on analytical limit of detction of ~0.1 μg HDI/TRIG per sample with sample volumes ranging from 20 to 150 L.
[A]TRIG calculated without HDI monomer.

on the surfaces of the vessel containing the test atmosphere of TDI and water vapor.[21,22] The authors' experience is that significant amounts of TDI adsorb onto and saturate available surfaces, as indicated by the time required to reach steady-state airborne concentrations in various test systems. The question arises as to whether this surface affinity is important when TDI exists in a mixed atmosphere with particulate matter. It may be postulated that vapor phase TDI would be in equilibrium with significant amounts of TDI adsorbed onto the particle surfaces. Similar behavior could be anticipated for other forms of TRIG, particularly in association with paint overspray aerosols. This work has clearly shown that in such circumstances, HDI monomer tends to partition between the vapor and condensed phases (approximately 80% vapor and 20% particulate).

The partitioning of TRIG into vapor and aerosol fractions may be important in relation to possible health effects of overexposure. The deposition pattern of the isocyanates during inhalation has not yet been determined, although it could be speculated that adsorption/deposition occurs down the length of the respiratory tract. Thus, it is possible that in certain circumstances little isocyanate in the vapor phase ultimately reaches the alveolar compartment. On the other hand, if the same isocyanate were present as respirable sized condensation aerosol or were adsorbed onto respirable particles, direct deposition in the alveoli would be enhanced. It is of interest to note that the majority of cases of hypersensitivity pneumonitis induced by diisocyanate exposure have

been associated with MDI, which the present authors and others have previously shown to partition into vapor and condensation aerosols at concentrations below the PEL.[10,20,23] The requirement of deposition of the antigen in the lower respiratory tract for induction of hypersensitivity pneumonitis, coupled with the existence of MDI as an aerosol, points up the importance of the physical state of the diisocyanates in their observed toxicities. In contrast to hypersensitivity pneumonitis, the induction of extrinsic asthma should not require this intimate contact of the etiologic agent with the deepest parts of the respiratory system.

Recognition of the physical state of an isocyanate is an important factor in the proper selection of appropriate collection and analysis techniques. The use of combinations of an untreated filter with a treated filter or impinger has been suggested for sampling of TRIG in mixed vapor/aerosol atmospheres.[23–26] However, this approach is inappropriate for accurate dichotomous sampling of isocyanates. Due to the significant vapor pressures of the isocyanate monomers, they tend to vaporize from untreated filters when sampling continues in a less than saturated atmosphere. In addition, the reactive nature of the isocyanate group dictates using a technique that rapidly stabilizes it as a chemical derivative on collection. Treating the filter to achieve the latter would result in efficient collection of the vapors along with the aerosols, negating the ability to differentiate between the phases. Thus, a specialized sampling apparatus is needed for dichotomous collection of mixtures of vapor- and condensed-phase TRIG.

In this work, diffusional denuder sampling has been applied to dichotomous measurement of TRIG. The diffusional denuder takes advantage of the huge difference in diffusivity of gases and submicrometer particles to effect a quantitative separation of the two. Thus, by using a flow column in which the wall acts as a perfect adsorbent, gases diffuse from the sample during passage and collect on the wall, whereas, due to their much smaller diffusivities, particles pass through and are collected by a final filtration device. Original designs of denuder tubes used simple flow tubes for construction; more recent designs use an annular denuder consisting of coaxial inner and outer cylinders, with the air flowing through the annular space between. The annular configuration provides the advantages of much higher flow rates, shorter column lengths, and improved collection efficiencies as compared with the tubular denuder.

The design of the annular denuder requires a preseparator to remove large particles from the flow stream, which could deposit on the denuder walls and bias the analytical results for the vapor fraction. There is the possibility that HDI present in nonrespirable aerosols that have deposited on the impactor or cyclone preseparator could subsequently volatilize, as it may with an untreated filter presampler used in other dichotomous samplers. However, the design of the cyclone, in particular, effectively removes the deposited particles from the flow stream. This should minimize the tendency of any HDI in the collected aerosol to volatilize. Thus, overall the annular denuder-based sampling device described in this work appears to be the most appropriate technique currently available for dichotomous sampling of TRIG vapor and aerosol.

CONCLUSIONS

An underlying hypothesis of this work was that certain isocyanates would exhibit a tendency to partition between vapor and aerosol/condensed phases as a function of concentration, method of generation, and inherent volatility. The dichotomous sampler developed in this work separated and independently quantitated vapor and aerosol fractions of HDI-derived TRIG in the laboratory and in an actual workplace. The performance of the optimized device was consistent with that predicted from theory and corresponded with independent measures of vapor and aerosol isocyanate. Evidence provided by the dichotomous sampler of partitioning of HDI in the laboratory and in the field clearly illustrated the significance of this phenomenon, and as a result has generated new questions concerning the behavior of isocyanates in the workplace environment. The results of this project point out the need for further research on the identity and behavior of TRIG in workplace atmospheres. Also, this new technique for measurement of TRIG should prove particularly useful in the conduct of epidemiologic assessments of exposed working populations, in an effort to identify and quantify the risks associated with occupational exposure to mixtures of TRIG vapor and aerosol.

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