

Determination of complex mixtures of airborne isocyanates and amines

Part 4.[†] Determination of aliphatic isocyanates as dibutylamine derivatives using liquid chromatography and mass spectrometry

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An LC–MS method is presented for the determination of aliphatic isocyanate [hexamethylene diisocyanate] (HDI), isophorone diisocyanate (IPDI), biuret and isocyanurate] adducts of HDI as their dibutylamine (DBA) derivatives. The method is based on sampling in midjet impinger flasks containing 10 ml of 0.01 mol l⁻¹ DBA in toluene (see parts 1–3 of this series[†]). The excess reagent and the solvent are removed by evaporation. The enriched samples are then analysed using LC–electrospray MS. Quantification of HDI–DBA and IPDI–DBA was effected by monitoring the molecular ion [MH]⁺. Linear calibration graphs were obtained in the range 50–500 nmol l⁻¹ with correlation coefficients of 0.9965–0.9997. The RSD for samples spiked at a concentration of 1 nmol l⁻¹ was 1.7 and 2.9% for the two IPDI–DBA isomers (*n* = 8) and 1.2% for HDI–DBA (*n* = 8). On injecting 4 µl of the 0.5 ml sample, the instrumental detection limit was about 20 nmol l⁻¹, which corresponds to about 0.1 µg m⁻³ for HDI and 0.2 µg m⁻³ for IPDI for a 15 l air sample.

No degradation was observed after storage of the derivatives for up to 4 months in acetonitrile or toluene. No losses were seen when the derivatization reaction took place in the presence of interferents such as morpholine, hexamethylenediamine, isophoronediamine and phenol corresponding to concentrations of 10 ppm in air for a 15 l air sample. The influence of water was studied by spiking with volumes corresponding to a relative humidity of 80% at 30 °C in 15 l of air. The reaction rates of HDI and IPDI with DBA were found to be 2–3 times faster than those for 1-(2-methoxyphenyl)piperazine.

Keywords: Airborne isocyanate–amine mixtures; aliphatic isocyanates; dibutylamine derivatives; liquid chromatography; mass spectrometry

Diisocyanates are mainly used for the production of polyurethane (PUR). PUR products have a wide range of applications, such as in rigid foams, coatings and elastomers. PUR products based on aliphatic isocyanates are mainly used as lacquers and two-component paints. Both aliphatic and aromatic isocyanates are well known occupational hazards and exposure can result in a variety of respiratory effects.^{1–3} To reduce the vapour pressure of hexamethylene diisocyanate (HDI) and isophorone diisocyanate (IPDI), they often occur in prepolymerized forms or as biuret or isocyanurate adducts. Technical grade aliphatic

isocyanates often contain mixtures of many kinds of isocyanates and degradation products. Liquid chromatography (LC) and mass spectrometry (MS) have been demonstrated to be useful tools for the analysis of complex aromatic isocyanates.^{4–6} They may be useful for aliphatic isocyanates, especially since reference compounds are lacking for many of the compounds of interest.

Several reagents and methods have been presented for the determination of aliphatic diisocyanates.^{7–10} However, information about reaction rates and stability of the methods towards interfering compounds is limited. Losses due to interferents have, however, been described for 1-(2-methoxyphenyl)piperazine (2MP) and 9-(*N*-methylaminomethyl)anthracene (MAMA) as derivatizing reagents for toluene diisocyanate (TDI).¹¹ In Parts 1–3 of this series, methods for the determination of aromatic isocyanates in air using dibutylamine (DBA) as the derivatization reagent followed by LC and UV and electrospray (ESP) MS detection were described. Fast reaction rates between isocyanates and DBA were demonstrated and the methods were found to be robust, with no influence of interfering compounds. In addition to the determination of aromatic isocyanates, aminoisocyanates and aromatic amines were also determined by the reaction of amine groups with ethyl chloroformate (ET). The aim of this study was to apply the DBA reagent to the determination of aliphatic isocyanates with special focus on HDI and IPDI, and to develop a reliable and sensitive method based on micro-LC and ESP-MS.

Experimental

Apparatus

LC–MS

A Quattro quadrupole mass spectrometer (VG Organics, Altrincham, Cheshire, UK) was used in the electrospray mode monitoring positive ions. The cone voltage was 50 V and the temperature of the ion source was 120 °C. Selected ion recording was performed by monitoring three ions with a dwell time of 0.2 s. Full continuous mass spectra from 100–1600 *u* were obtained during 4 s and were refined by maximum entropy reconstruction. Tetradeuterium-labelled HDI–DBA (THDI–DBA) was used as an internal standard. Quantitative measurements were made by monitoring positive ions (ESP⁺ *m/z* = MH⁺). The mass spectrometer was connected to a Phoenix 40 micro-LC pump (Fisons Instruments, Carlo Erba, Milan, Italy). Partially filled loop injections of 4 µl in a 9.6 µl loop volume containing 5.6 µl of wash liquid consisting of acetonitrile–water (1 + 1 v/v) were made with a CMA/200 refrigerated autosampler (Carnegie, Stockholm, Sweden).

[†] For Parts 1–3 of this series, see refs. 4–6.

The DBA–isocyanate derivatives were analysed using gradient elution for 35 min with a mobile phase of acetonitrile–water (from 1 + 1 to 95 + 5 v/v) containing 0.05% formic acid. The LC column was a Hypersil C₁₈ (150 × 1.0 mm id with 5 µm particles) (Hypersil, Cheshire, UK).

Air sampling

Air sampling was performed using a Model 224 universal sampler (SKC, Eighty Four, PA, USA). Midget impinger flasks (30 ml) containing 10 ml of 0.01 mol l⁻¹ DBA were used. Air flows (1 l min⁻¹) were measured with a Gilibrator bubble flow meter (Gilian Instruments, Clearwater, IL, USA).

LC-UV

A Model 600 multi-solvent delivery system and a Model 490 programmable multi-wavelength detector ($\lambda = 242$ nm) (Millipore–Waters, Milford, MA, USA) was used. Injections were made with a CMA/200 refrigerated autosampler. The loop volume was 20 µl. Chromatograms were evaluated using Elds Professional (Chromatography Data Systems, Stockholm, Sweden).

The 2MP derivatives of isocyanates were determined using isocratic elution with a mobile phase of acetonitrile–aqueous sodium acetate (6 + 4, v/v) at pH 6. The column used for LC–UV was a Supelcosil LC18 (150 × 2.1 mm id with 5 µm particles) (Supelco, Bellefonte, PA, USA).

The samples were evaporated at 40 °C in a Speed Vac 290 centrifuge evaporator (Savant, Farmingdale, NY, USA).

Chemicals

Toluene, isooctane and HPLC-grade acetonitrile were obtained from Lab-Scan (Dublin, Ireland), DBA, IPDI and 2MP from Aldrich Chemie (Steinheim, Germany), HDI from Janssen Chimica (Beerse, Belgium), morpholine from Sigma (St. Louis, MO, USA), phenol, hexamethylenediamine (HDA) and formic acid from Merck (Darmstadt, Germany), isophoronediamine (IPDA) from TCI (Tokyo, Japan), ethanol from Kemetyl (Stockholm, Sweden), tetradeuterium-labelled HDA from MSD Isotopes (Merck Frosst Canada, Montreal, Canada), HDI–biuret and –isocyanurate adducts from Bayer (Leverkusen, Germany) and diethylamine (DEA) from Riedel-de Haën (Seelze, Germany).

Synthesis of HDI–DBA and IPDI–DBA derivatives

The syntheses were carried out according to the methods for aromatic isocyanates presented in Parts 1–3.^{4–6} An amount of 0.9 g of HDI or 1.1 g of IPDI (5.4 mmol) was dissolved in 25 ml of isooctane and 8 g of DBA (62 mmol) was dissolved in 25 ml of toluene. The isocyanate solution was added dropwise to the DBA solution with continuous stirring. The organic solvents and the excess of DBA were removed by evaporation to dryness with a rotary evaporator. The precipitate was then further dried in a vacuum desiccator.

Synthesis of tetradeuterium-labelled HDA–ET (THDA–ET)

An amount of 0.3 g (1.7 mmol) of tetradeuterated HDA was dissolved in 20 ml of toluene. Thereafter, 150 µl pyridine and 40 ml of 5 mol l⁻¹ NaOH were added to the solution. Ethyl chloroformate (1.5 ml) was then added dropwise under continuous stirring. After 10 min, the toluene phase was separated. The toluene was then shaken with 0.1 mol l⁻¹ HCl. The precipitate was dried and kept in a vacuum desiccator.

Synthesis of tetradeuterium-labelled HDI–DBA

Tetradeuterium labelled HDI (THDI) was formed by thermal decomposition of THDA–ET. About 20 mg of THDA–ET was placed in a glass tube. The tube, heated to about 300 °C, was connected to a 3 m piece of stainless-steel tubing (2–3 mm id) in an oven at 350 °C. The gaseous THDI was collected (1.5 l min⁻¹) in an impinger flask containing DBA in toluene (0.5 mol l⁻¹), whereupon tetradeuterium labelled HDI–DBA (THDI–DBA) was formed. The toluene solution was evaporated to dryness and the dry residue was dissolved in acetonitrile.

Work-up procedure

Sample solutions containing the isocyanate–DBA derivatives were evaporated to dryness in a vacuum centrifuge. The dry residues were dissolved in 0.5 ml of acetonitrile containing about 100 µg l⁻¹ of THDI–DBA.

Sample solutions containing the isocyanate–2MP derivatives were evaporated to dryness in a vacuum centrifuge. The dry residues were dissolved in 1 ml of 0.5% anhydrous acetic acid in acetonitrile.

Interferences

The reactions between HDI and IPDI with DBA in the presence of some possible interfering compounds were investigated. The reactions were studied separately for the two isocyanates with each of the possible interferents. Test-tubes containing 10 ml of 0.01 mol l⁻¹ DBA in toluene were spiked with 6.2 µmol, corresponding to 10 ppm in air and a 15 l air sample, of morpholine, phenol, ethanol, HDA and IPDA. The influence of water was studied by spiking samples with 150 µl of water, corresponding to the water content in 15 l of air with a relative humidity of 80% at 30 °C. To the spiked test-tubes, 3.7 nmol of HDI and IPDI were added. After about 1 h, the HDA and IPDA spiked solutions were extracted with aqueous phosphate buffer (pH 2) to remove HDA and IPDA.

Kinetics

The reaction rates during 16 h of HDI and IPDI with DBA were investigated by mixing isocyanates in toluene (25 ml, 42 µmol l⁻¹) and DBA in toluene (25 ml, 126 µmol l⁻¹). Aliquots of 1.5 ml were taken from the reaction mixture, at appropriate intervals, and placed in test-tubes containing a large excess of DEA (1 ml, 6.3 mmol l⁻¹), whereby the reaction with DBA was stopped.

The reaction rate during 16 h for HDI and IPDI with 2MP was investigated by mixing isocyanates in toluene (25 ml, 42 µmol l⁻¹) and 2MP in toluene (25 ml, 126 µmol l⁻¹). Aliquots of 1.5 ml were taken from the reaction mixture, at appropriate intervals, and placed in test-tubes containing a large excess of DBA (1 ml, 6.3 mmol l⁻¹), whereby the reaction with 2MP was stopped.

The reactions were studied at ambient temperature (24.6–26.7 °C). An approximation of the completely reacted isocyanate ($t \rightarrow \infty$) was estimated by the addition of a 15-fold excess of DBA or 2MP to aliquots taken after about 3 h.

Results

Stability of the HDI– and IPDI–DBA derivatives

Within the experimental errors, no degradation was observed for samples containing 10 µmol l⁻¹ of each of the HDI– and

IPDI-DBA derivatives in toluene or acetonitrile, in either light or dark, after storage for up to 4 months.

Interferences

No losses of HDI and IPDI were observed for any of the interferences studied. Compared with HDI- and IPDI-spiked DBA solutions, containing no interferent, 94–110% of IPDI₁, 95–114% of IPDI₂ and 98–102% of HDI were found in the samples containing interferences. The greater deviations found for IPDI are due to the poorer reproducibility and repeatability as THDI-DBA was used as the internal standard.

Kinetics

The reactions between the isocyanates and the DBA and 2MP reagents follow second-order reaction patterns (Fig. 1). It was found that 50% of the HDI-, IPDI₁- and IPDI₂-DBA derivatives were formed after 80, 90 and 110 min, respectively. The reactions were complete within 1000 min. Also, 50% of the HDI-, IPDI₁- and IPDI₂-2MP derivatives were formed after 170, 210 and 220 min, respectively. Within 1000 min about 90% complete formation of the derivatives was observed. The reactions between the isocyanates and DBA were found to be about 2–3 times faster than those for 2MP, at a similar temperature and concentration of reactants.

Chromatography

Gradient LC-ESP-MS of the studied aliphatic isocyanates showed symmetrical peaks with good separation (Fig. 2). Injections were performed using the column focusing technique as presented in Parts 2–3,^{4,5} and about 40 injections were made during 24 h. The HDI-biuret and the HDI-isocyanurate adducts were observed at high levels and traces of HDI were seen. In the chromatograms, three other compounds at high levels were also seen. These are attributed to derivatives of the HDI dimer (uretidone) adduct, the isocyanurate-uretidone adduct and HDI-diisocyanurate. Schematic structural formulae are illustrated in Fig. 3. The elution order followed the order of increasing molecular mass and the number of isocyanate-DBA urea groups in the compounds. The tetradeuterium-labelled HDI-DBA eluted a few seconds earlier than HDI-DBA. The same components were observed in chromatograms of the air samples and from the isocyanate component used.

The RSDs of the retention times of HDI-, IPDI₁- and IPDI₂-DBA were 0.12, 0.08 and 0.07% ($n = 10$), respectively, and the RSDs of the relative retention times were 0.06, 0.08 and 0.16%, respectively. A chromophore is not present in the aliphatic

isocyanate DBA derivatives and therefore they are not observed on the LC-UV traces.

Mass spectrometry

ESP ionization with positive ion monitoring was studied for IPDI-DBA, HDI-DBA, HDI-isocyanurate-DBA and HDI-biuret-DBA, which are available as references (Fig. 4). In all the spectra, the following typical ions appear: MH^+ ($M + 1$ u), MNa^+ ($M + 23$ u), $[MH - DBA]^+$ ($MH -$ dibutylamine fragment, $M - 129$ u), $[DBAH]^+$ (protonated dibutylamine, 130 u) and $[DBACO]^+$ (dibutylaminocarbonyl fragment, 156 u). The HDI-biuret-DBA spectrum [Fig. 4(C)] is more complex and contains the following m/z peaks: 582 ($MH - 284$, $MH - H_2NC_6H_{12}NHCONHC_6H_{12}NCO$); 569 ($MH - 297$, $MH -$

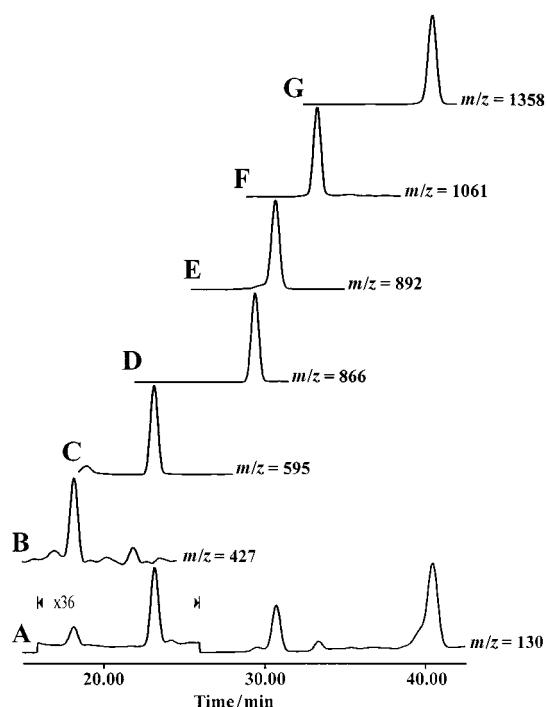


Fig. 2 Micro-LC-ESP⁺-SIR chromatograms of airborne aliphatic isocyanates. The 6 l (1 l min⁻¹) sample was taken in a car-painting workshop during spray painting. The presence of six different isocyanates was observed. Chromatogram A indicates the aliphatic isocyanate DBA + 1 ions. The $M + 1$ ions are seen in the chromatograms of: B, HDI-DBA; C, HDI-dimer (uretidone)-DBA; D, HDI-biuret-DBA; E, HDI-isocyanurate-DBA; F, HDI-isocyanurate-uretidone-DBA; and G, HDI-diisocyanurate-DBA. The scale is adjusted to show the same peak ESP⁺. The HDI-DBA peak reflects an air concentration of about 2 $\mu\text{g m}^{-3}$.

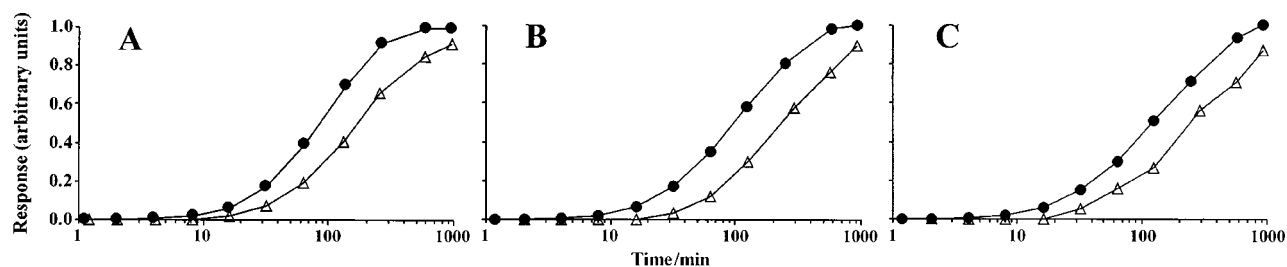


Fig. 1 Formation of diurea derivatives of aliphatic diisocyanates with DBA and 2MP versus time: A, HDI-DBA (●) and HDI-2MP (Δ); B, IPDI₁-DBA (●) and IPDI₁-2MP (Δ); and C, IPDI₂-DBA (●) and IPDI₂-2MP (Δ). The reactions were performed in toluene at room temperature by mixing equal volumes of 46 $\mu\text{mol l}^{-1}$ HDI or IPDI (IPDI₁ + IPDI₂) with 126 $\mu\text{mol l}^{-1}$ of DBA or 2MP. The response (1.0) reflects the formation of the derivatives when time $t \rightarrow \infty$.

NCOC₆H₁₂NCODBA); 453 (MH-413, MH - DBANCO-CONC₆H₁₂NCODBA); 440 (MH - 426, MH - HDIDBA); 414 (MH - 452, MH - H₂NC₆H₁₂NHCONHC₆H₁₂NCODBA); 311 (MH - 555, OCNC₆H₁₂NHCONHC₆H₁₂NCO); 298 (MH - 568, OCNC₆H₁₂NCODBAH); 285 (MH - 581, H₂NC₆H₁₂NHCONHC₆H₁₂NCO); 272 (MH - 594, H₂NC₆H₁₂NCODBAH); and 143 (H₂NC₆H₁₂NCOH). The HDI-isocyanurate spectrum [Fig. 4(D)] contains the following *m/z* peaks: 634 (M - 258, MH - 2DBA); 608 (MH - 284, MH - H₂NC₆H₁₂NHCONHC₆H₁₂NCO); 479 (MH - 413, MH - H₂NC₆H₁₂NHCONHC₆H₁₂NCODBA); and 382 (M - 129; doubly charged, see below).

The mass spectra of the DBA derivatives of the HDI-isocyanurate adduct and HDI-biuret adduct, in the air sample from a car paint shop (Fig. 2), were identical with those of the reference derivatives. In addition, at least three other aliphatic isocyanates were observed, corresponding to the HDI dimer (uretidone), the HDI-diisocyanurate and the HDI-uretidone-isocyanurate [Fig. 3(E) and (G)]. The presence of the HDI dimer adduct is indicated by the presence of the molecular ion at *m/z* = 595 u [Fig. 5(A)]. In addition, the spectrum contains the following *m/z* peaks: 130, 156, 298 (MH - 297, HDIDBA) and 466 (MH - 129, MH - DBA). The fragmentation pattern is similar to that for HDI-DBA. The presence of the isocyanurate-

uretidone adduct is indicated by the presence of the MH⁺ ion of 1061 u [Fig. 5(B)]. Typical ions that are present in the HDI-isocyanurate and the HDI-uretidone spectra are also found in the isocyanurate-uretidone spectrum: *m/z* 130, 156, 932 (MH - 129), 906 (MH - 155), 803 (MH - 258), 777 (MH-284), 764 (MH-297), 635 (MH-426), 609 (MH-452), 480 (MH - 581) and 298 (HDIDBAH). This strongly indicates the presence of HDI-isocyanurate-uretidone in the air sample. The presence of the HDI-diisocyanurate is indicated by the presence of the M + 1 ion at *m/z* = 1358. Other ions which appear are at *m/z* 1229 (MH - 129), 1203 (MH - 155), 1100 (MH - 258), 1074 (MH - 284), 970 (MH - 388) and 945 (MH - 413), [Fig. 5(C)]. These are all found in the HDI-isocyanurate spectra. In addition, two ions at *m/z* = 815 (MH - 543) and 790 (MH - 568) were also seen. Three doubly charged ions were observed: the molecular MH₂²⁺ and [MH₂ - 129]²⁺ and [MH₂ - 258]²⁺ ions. The doubly charged ions were indicated by the presence of the typical isotopic cluster where the fragments are 0.5 u apart as compared with singly charged ions which are 1 u apart (Fig. 6). Notably, the natural occurrence of ¹³C, which is about 1%, clearly influences the relative abundance of the different related ions in the ion clusters. The relative abundance for the 615.8 u ion in Fig. 6(A) is about 65%, which is as expected as the molecule contains 64 carbon atoms, whereas the relative

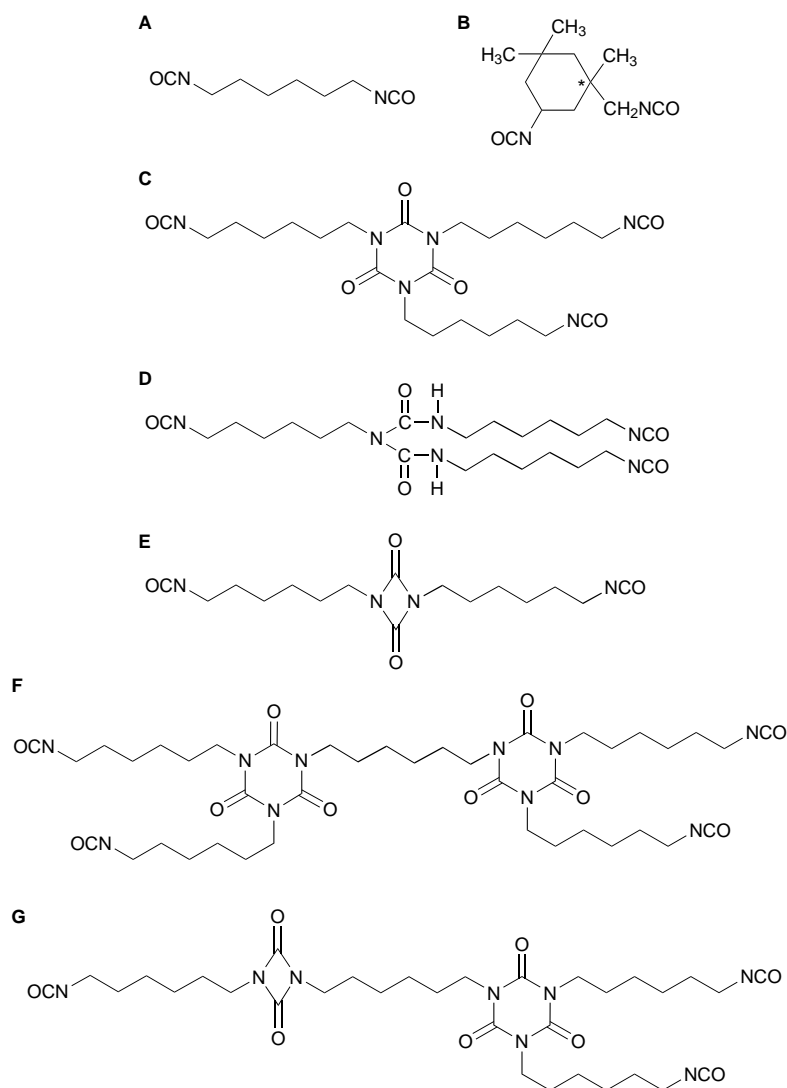


Fig. 3 Structures of some common aliphatic isocyanates used in lacquers for car painting: A, HDI; B, IPDI; C, HDI-isocyanurate adduct; D, HDI-biuret adduct; E, HDI-dimer (uretidone); F, HDI-diisocyanurate adduct; and G, HDI-isocyanurate-uretidone adduct.

abundance of the 480.7 u ion in Fig. 6(B) is about 25%, which is as expected as the molecule contains 24 carbon atoms.

The abundance and the relative abundance of the ions are greatly affected by the applied cone voltage (Fig. 7). For quantification, the MH^+ ions were monitored and the optimum cone voltage was about 40–50 V. The ion source needed to be rinsed only once a month.

Quantification

Aliquots of 10 ml of toluene solutions containing 0.01 mol l^{-1} DBA were spiked with HDI and IPDI at six concentrations in the range of 50–500 nmol l^{-1} . The work-up procedure was then performed (20-fold enrichment). Peak area selected ion recording (SIR) measurements were made. Virtually linear calibration graphs were obtained with correlation coefficients of 0.9997 for HDI–DBA, 0.9965 for IPDI₁–DBA and 0.9990 for IPDI₂–DBA. The precisions (RSDs) for peak area ratio measurements on eight samples spiked with 1 nmol ml^{-1} each of HDI–DBA, IPDI₁–DBA and IPDI₂–DBA were 1.2, 1.7 and 2.9% respectively. The precisions for peak area measurements were 4.7, 3.0 and 6.0%, respectively.

The instrumental detection limit, defined as three times the noise, was about 20 nmol l^{-1} , which corresponds to about $0.11 \text{ } \mu\text{g m}^{-3}$ for HDI and $0.15 \text{ } \mu\text{g m}^{-3}$ for IPDI, in a 15 l air sample. The instrumental detection limit for full-scan MS determinations was about 200 nmol l^{-1} .

Application

Air samples were collected ($n = 10$) at a car-painting workshop during a spray painting operation. In chromatograms representing the isocyanate component used, several isocyanates were observed in the chromatograms. Samples were taken at approximately 0.5 m behind the spray gun, during short periods of time (3–6 min). The total concentrations of isocyanates in air were at the mg m^{-3} level. HDI was also observed (in air

$< 10 \text{ } \mu\text{g m}^{-3}$). The worker involved was using a personal respiratory protection device.

Discussion

Two of the most dominant aliphatic diisocyanate monomers in the PUR industry have been studied in some detail. The method has also been applied to biuret, uretidone and isocyanurate adducts. In the industry, many other kinds of aliphatic isocyanates are present. There is only limited information in the literature regarding the different toxicities of the various aliphatic isocyanates. To achieve better information regarding the health hazard associated with different kinds of isocyanates, more and better quality exposure data are needed. Safety data sheets on various isocyanate components typically contain only limited chemical information and essentially the same data sheets are used for different qualities. For the worker the information may be sufficient for the choice of the best type of respiratory protection device. It may be misleading for the analytical chemist, however, and there is a risk of underestimating the total isocyanate content in air. We were surprised to see so many chemical isocyanate variants in the samples. Numerous different qualities of isocyanates are used to obtain different characteristics of the polymerization reaction and of the lacquer. To analyse complex isocyanates and isomers, the best available LC separation technique and detection methods are necessary. In this case, full-scan MS runs are necessary. The formation of typical ions such as the $m/z = 130$ ion greatly facilitates the interpretation of the mass spectra. A certain practical problem arises, as the file sizes of continuous mass spectra are enormous. During one day, several gigabytes of data are produced.

It is essential for the analytical chemist to have access to reference compounds, especially for quantification, but these are available for only a few isocyanates. The data regarding the reaction kinetics between aliphatic isocyanates presented in this paper were studied for DBA and 2MP at concentrations of $126 \text{ } \mu\text{mol l}^{-1}$ for practical reasons. In the work-up procedure, the concentration of DBA is 0.01 mol l^{-1} , which is about 100

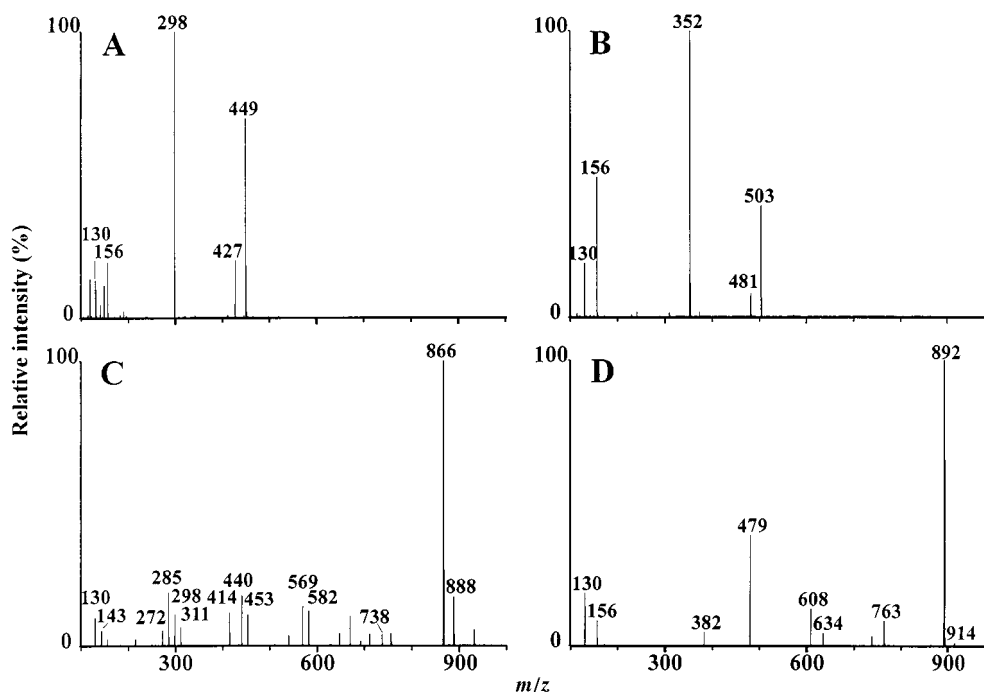


Fig. 4 ESP⁺ reconstructed mass spectra of: A, HDI–DBA; B, IPDI–DBA; C, HDI–biuret–DBA; and D, HDI–isocyanurate–DBA.

times higher. At this concentration, the reaction rate is very fast and it is not possible to study the time dependence of the

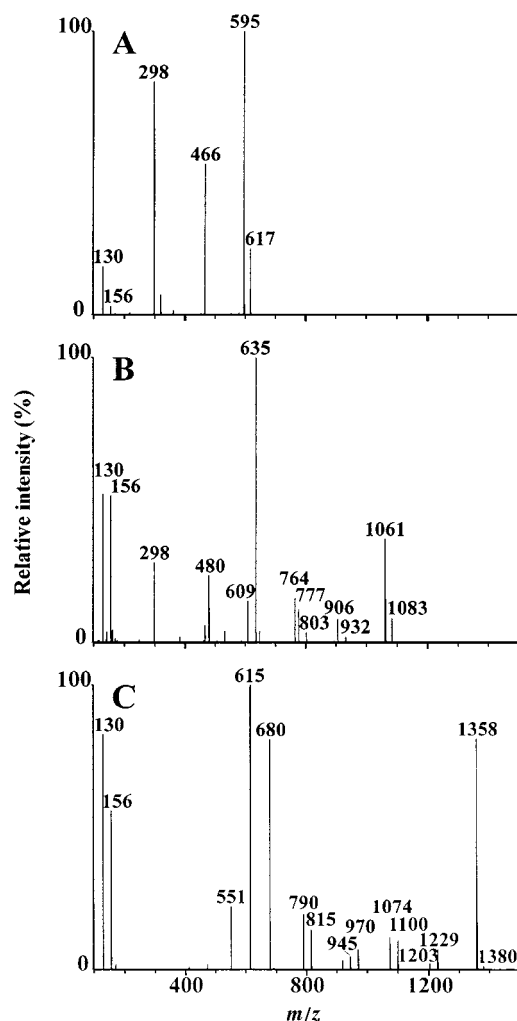


Fig. 5 ESP+ reconstructed mass spectra of three aliphatic isocyanates found in air samples from a car paint shop: A, HDI-dimer (uretidone)-DBA; B, HDI-isocyanurate-uretidone-DBA; and C, HDI-diisocyanurate-DBA.

reactions. The robustness of the method was demonstrated by the lack of noticeable interference from the interferents tested. The studied concentration of 2MP was of the same order of magnitude as that described for the 2MP method. Earlier we presented data regarding 2MP and the influence of interfering compounds for aromatic isocyanates. Owing due to the slow reaction rate for aliphatic isocyanates, there are reasons to believe that aliphatic isocyanates may be affected by interfering compounds when 2MP is used as a reagent.

In Parts 2 and 3,^{2,3} micro-LC was demonstrated to enhance the chromatography and improve the detection limits. The instrumentation used there was modified conventional LC equipment using a split technique to achieve sufficiently low flow rates. In this study, dedicated micro-LC equipment was used and a greatly improved chromatographic performance was achieved. The RSDs of the retention times were improved about fivefold.¹² The introduction of deuterium-labelled isocyanate derivative internal standards and the development of a method to synthesise isocyanates and derivatives thereof greatly facilitate the quantification. This is demonstrated by the good precision achieved for HDI-DBA. The RSDs for the two IPDI-DBA derivatives were not as good as for HDI-DBA owing to the use of tetradeuterium-labelled HDI-DBA as the internal standard. This clearly demonstrates that the proper choice of an internal standard greatly affects the quantification. In the work-up procedure, an enrichment factor of 20 is described. As the DBA reagent is almost completely removed, further enrichment can be achieved. Further enrichment is useful when choosing to obtain full spectra of isocyanates of special interest, such as the unknown ones, or when determining isocyanates with short sampling times or at extremely low concentrations at < 1% of the threshold limit value (TLV), in this case using SIR. The proper choice of the internal standard is much more important when the enrichment factor is increased. The detection limit for a final sample volume of 10 μ l and a 15 l air sample will correspond to detection limits of < 0.05% of the TLV. This detection limit can be lowered even further by lowering the MS resolution and by the optimization of the conditions of the LC-MS interface.

Conclusion

LC-MS has been demonstrated to be a valuable tool for the determination of airborne isocyanates. The reaction between

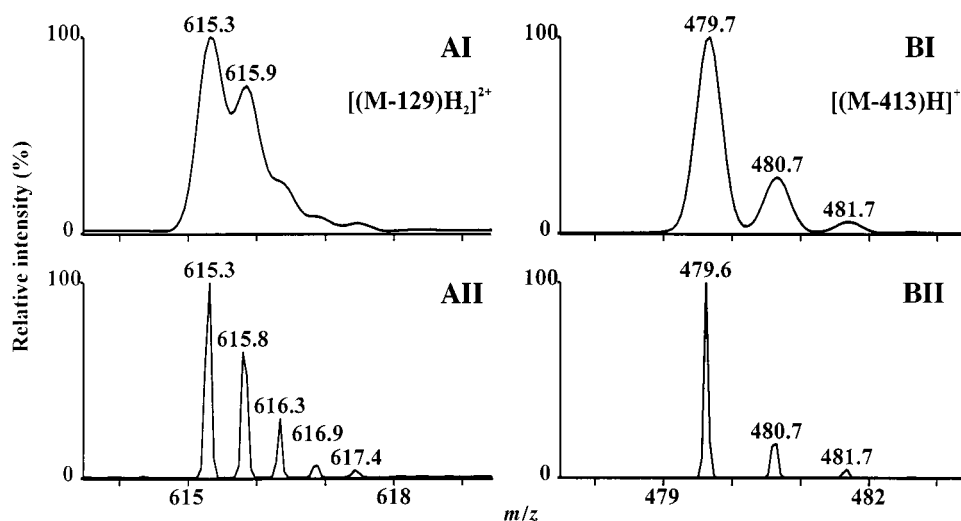


Fig. 6 Continuous mass spectra of: A, HDI-diisocyanurate ($M = 1358$ u), doubly charged $m/z = 615$ ion, ($C_{64}H_{119}N_{13}O_{10}$)²⁺, smoothed spectra (I) and maxentropy reconstructed mass spectra (II); and B, HDI-isocyanurate ($M = 892$ u), singly charged $m/z = 479$ ion, ($C_{26}H_{47}N_4O_4$)⁺, smoothed spectra (I) and maxentropy reconstructed mass spectra (II).

DBA and aliphatic isocyanates is robust with respect to the possible competing reactions with compounds that are typically

present in the work environment. The removal of the reagent during the work-up procedure greatly facilitates the subsequent chromatographic determination. The use of deuterium-labelled internal standards improves the quantification. LC-MS of air samples from a paint shop demonstrated the presence of many isocyanate components. As a great number of workers are exposed, and there is a well known risk of respiratory disorder, more knowledge regarding exposure is necessary. Even when using sophisticated equipment, there is an immediate need for reference compounds for the determination of the large number of different aliphatic isocyanates found in the PUR industry.

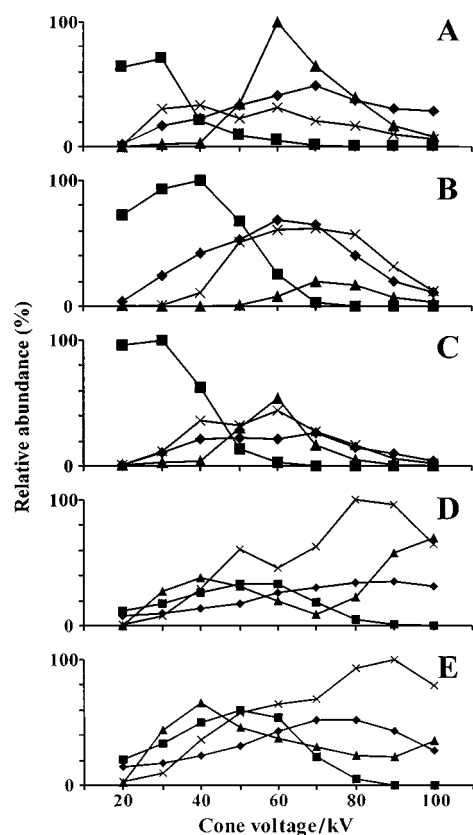


Fig. 7 Influence of cone voltage on the ESP⁺ fragmentation of aliphatic isocyanate DBA derivatives. A, HDI-DBA; B, IPDI₁-DBA; C, IPDI₂-DBA; D, HDI-biuret-DBA; E, HDI-isocyanurate-DBA. ◆, (M + 23)⁺; ■, (M + 1)⁺; ▲, $m/z = 156$; and ×, $m/z = 130$.

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