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Workplace atmospheres — Determination of total isocyanate groups in air using 1-(9-anthracenylmethyl)piperazine (MAP) reagent and liquid chromatography

Air des lieux de travail — Dosage des groupements isocyanates totaux dans l'air par réaction avec la 1-(9-anthracénylméthyl)pipérazine (MAP) et par chromatographie en phase liquide

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Foreword

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The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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ISO 17735 was prepared by Technical Committee ISO/TC 146, *Air quality*, Subcommittee SC 2, *Workplace atmospheres*.

Introduction

This International Standard specifies the use of 1-(9-anthracenylmethyl)piperazine (MAP) to measure monomeric and oligomeric isocyanate species in workplace atmospheres. MAP was designed to improve the reliability of identification of isocyanate species in sample chromatograms and to improve the accuracy of quantification of these species relative to established reagents. The high performance liquid chromatography (HPLC) analysis uses a pH gradient to selectively accelerate the elution of MAP derivatives of oligomeric isocyanates that might be unobservable in an isocratic analysis. The performance of MAP has been compared to other reagents used for total isocyanate analysis (Reference [7]). MAP has been found to react with phenyl isocyanate (used as a model isocyanate) as fast or faster than other reagents commonly used for isocyanate analysis. The UV response of MAP derivatives is comparable to that of 9-(methylaminomethyl)anthracene (MAMA) derivatives and considerably greater than other commonly used reagents [approximately three times greater than 1-(2-methoxyphenyl)piperazine (1-2MP) derivatives of aromatic isocyanates and 14 times greater than 1-2MP derivatives of aliphatic isocyanates]. The compound-to-compound variability of UV response per isocyanate group for MAP derivatives is smaller than the variability of any other commonly used reagent/detector combination (the coefficient of variation is 3,5 % for five model isocyanates). This results in accurate quantification of detectable non-monomeric isocyante species based on a calibration curve generated from analysing standards of monomeric species. The monomeric species used for calibration is generally the one associated with the product being analysed, but others could be used due to the very small compound-to-compound response variability of the MAP derivatives. The intensity of fluorescence response of MAP derivatives is comparable to that of MAMA derivatives and considerably greater than other reagents (e.g. approximately 30 times more intense than that of tryptamine derivatives). The compound-to-compound variability in fluorescence response has been found to be smaller than that of MAMA derivatives but larger than that of tryptamine derivatives (MAMA = 59 % coefficient of variation, MAP = 33 % coefficient of variation, and tryptamine = 16 % coefficient of variation for 5 model isocyanates). The compound-to-compound fluorescence variability of MAP derivatives is considered too great for accurate quantification of non-monomeric isocyanate species based on calibration with monomer standards. However, the sensitivity of the fluorescence detection makes it especially suitable for quantification of low levels of monomer, and the selectivity is very useful to designate an unidentified HPLC peak as a MAP derivative. MAP derivatives also give a strong response by electrochemical detection. The pH gradient used in the HPLC analysis selectively accelerates the elution of amines (MAP derivatives are amines), and is very strong (it accelerates MDI more than 100-fold). Re-equilibration to initial conditions is almost immediate. Many oligomeric species can be measured in the 30 min MAP analysis that may be unobservable in a much longer isocratic analysis.

MAP has been used in several studies comparing it side-by-side with other methods. Reference [8] found MAP impingers and NIOSH 5521 impingers (comparable to MDHS 25) to give comparable results in spray painting environments. Reference [8] used MAP reagent, but the pH gradient was not employed. Reference [9] compared MAP impingers with several other impinger methods (NIOSH 5521 and NIOSH 5522) and the double filter method. The average MAP oligomer value was substantially higher than the other impinger methods and slightly higher than the double filter method. The pH gradient was used in these MAP analyses.

The MAP method is currently available as NIOSH Method 5525 (Reference [11]). The performance characteristics of the method have been evaluated in Reference [12].

Workplace atmospheres — Determination of total isocyanate groups in air using 1-(9-anthracenylmethyl)piperazine (MAP) reagent and liquid chromatography

1 Scope

This International Standard gives general guidance for the sampling and analysis of airborne organic isocyanates in workplace air.

This International Standard is appropriate for a wide range of organic compounds containing isocyanate groups, including monofunctional isocyanates (e.g. phenyl isocyanate), diisocyanate monomers (e.g. 1,6-hexamethylene diisocyanate (HDI), toluene diisocyanate (TDI), 4,4'-diphenylmethane diisocyanate (MDI), and isophorone diisocyanate (IPDI), prepolymers (e.g. the biuret and isocyanurate of HDI), as well as intermediate products formed during production or thermal breakdown of polyurethane.

In mixed systems of HDI and IPDI products, it is impossible to identify and quantify low levels of IPDI monomer using this International Standard, due to coelution of IPDI monomer with HDI-uretidinedione.

The useful range of the method, expressed in moles of isocyanate group per species per sample, is approximately 1×10^{-10} to 2×10^{-7}.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 5725-2, *Accuracy (trueness and precision) of measurement methods and results — Part 2: Basic method for the determination of repeatability and reproducibility of a standard measurement method*

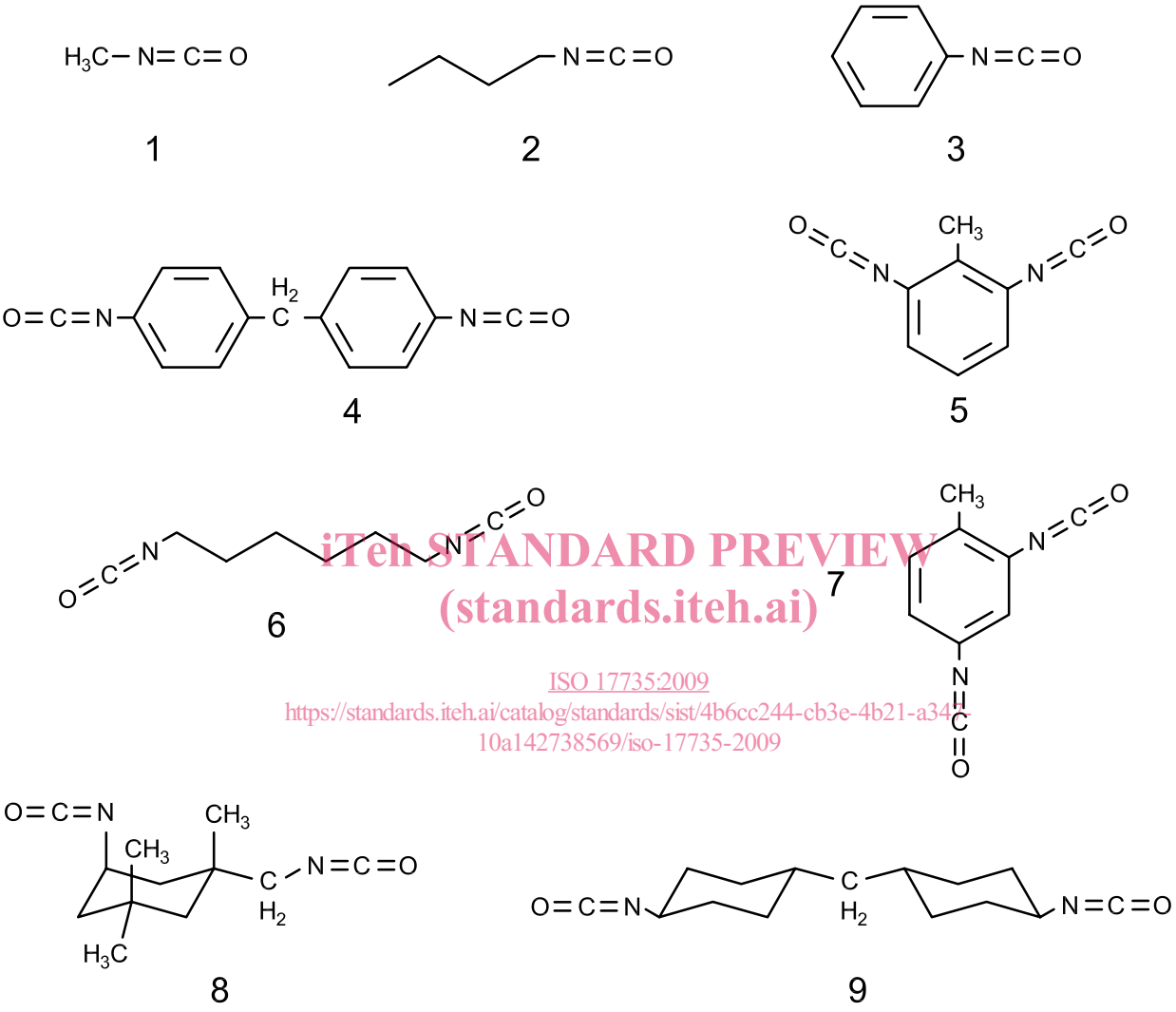
ISO 16200-1, *Workplace air quality — Sampling and analysis of volatile organic compounds by solvent desorption/gas chromatography — Part 1: Pumped sampling method*

3 Principle

A measured volume of air is drawn through either an impinger containing a solution of 1-(9-anthracenylmethyl)piperazine (MAP), a filter impregnated with MAP, or a sampling train consisting of an impinger followed by an impregnated filter. The choice of sampler depends on the chemical and physical characteristics of the airborne isocyanate (Reference [13]). If an impinger is used, the solution is subjected to solid-phase extraction (SPE) and the eluate is concentrated and analysed by reverse phase high performance liquid chromatography (HPLC) with ultraviolet (UV) absorbance and fluorescence (FL) detection in series. If an impregnated filter is used for sampling, it is extracted with solvent either in the field after completion of sampling or in the laboratory. Waiting to extract the filter until after the sample has been received by the analytical laboratory is acceptable only for analysis of isocyanates collected as vapour. This solution is filtered and analysed by HPLC/UV/FL. Isocyanate-derived peaks are identified based on their UV and FL responses and by comparison with the chromatogram of a derivatised bulk isocyanate product if available. Quantification of compounds for which analytical standards are available (generally monomers) is achieved by comparison

of the FL peak height of the sample peak with the FL peak height of standard matching solutions. Quantification of compounds for which analytical standards are not available is achieved by comparison of the UV area of the sample peak with the UV area of the appropriate monomer standard (i.e. the monomer from which the isocyanate product is derived).

Structures of some common diisocyanate monomers are shown in Figure 1.



Key

1 methyl isocyanate
2 butyl isocyanate
3 phenyl isocyanate
4 4,4'-MDI
5 2,6-TDI
6 HDI
7 2,4-TDI
8 IPDI
9 HMDI

Figure 1 — Structures of some common isocyanates

4 Reagents and materials

CAUTION — Observe appropriate safety precautions when preparing reagents. Carry out preparations under a fume hood to avoid exposure to solvents, isocyanates or other volatile reagents. Wear nitrile gloves when manipulating reagents and solvents.

During the analysis, unless otherwise stated, use only reagents of HPLC grade or better, and water of HPLC grade.

4.1 MAP reagent

MAP is prepared by the reaction of 9-(chloromethyl)anthracene with piperazine as shown in Figure 2.

The procedure using HPLC grade solvents is as follows.

Dissolve 10,8 mmol (2,47 g) of 9-(chloromethyl)anthracene (98 % mass fraction) in 25 ml methylene chloride. Place this solution in a dropping funnel.

Dissolve 54,4 mmol (4,69 g) of piperazine (99 % mass fraction) and 21,8 mmol (3,04 ml) of triethylamine (99,5 % mass fraction) in 37 ml methylene chloride. Place this solution in a 250 ml 2-necked round-bottomed flask with a magnetic stirring bar.

While stirring this solution, add the 9-(chloromethyl)anthracene solution dropwise over a 30 min period. Rinse down the dropping funnel with an additional 10 ml of methylene chloride. Allow the reaction to continue while stirring for at least 2 h.

Using a separating funnel, wash the reaction mixture three times with 130 ml water by shaking vigorously for 1 min. Discard the emulsion that forms after the first wash, which contains primarily an impurity and not MAP. Discard the aqueous washings.

Place the washed MAP solution in a weighed round-bottomed flask. Allow the methylene chloride to evaporate under a steady stream of nitrogen. Weigh the flask with the residue to obtain an approximate yield. This crude MAP can be safely stored in a freezer until further purification.

MAP is purified by column chromatography followed by sublimation. Using a glass chromatography column of internal diameter approximately 50 mm, add a slurry of silica gel in toluene until the silica gel bed is approximately 80 mm deep. Wash the sides of the column down with toluene and allow the toluene to run through the column until the toluene is even with the silica gel surface.

Dissolve the crude MAP in 80 ml of toluene. Sonicate the mixture for 5 min and filter through filter paper. Save the filtrate. Resuspend the residue in 20 ml toluene, sonicate for 5 min, and filter through filter paper. Discard the residue. Combine the filtrates and carefully load them onto the top of the silica gel bed. Pass an additional bed volume of toluene through the column. Discard the toluene eluate.

Begin to elute with ethyl acetate. Begin collecting 20 ml fractions in disposable vials with caps lined with polytetrafluoroethylene (PTFE). Monitor the fractions by spotting 1 µl of each on a thin layer chromatography (TLC) sheet (see below) and viewing the intensity of the spot under UV light after the solvent has evaporated. This procedure indicates the presence of compounds in the fraction, which may or may not be MAP. Elute with ethyl acetate until the yellow colour has been eluted, which requires about 400 ml ethyl acetate. The MAP should be completely retained on the column at this point. After elution of the yellow colour, begin eluting with methanol, which requires 1,0 l to 1,5 l methanol.

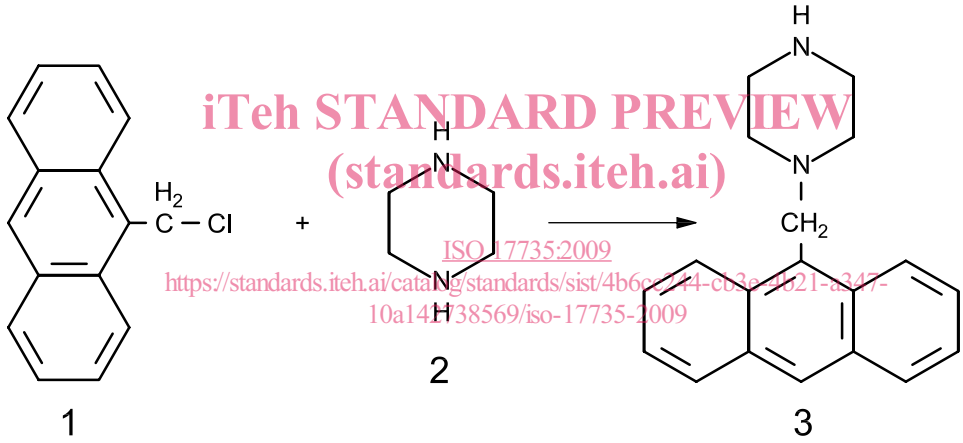
The elution of the MAP can be readily followed by TLC. A portion of the fractions that had given a significant spot on the TLC sheet are analysed by TLC to determine which fractions contain MAP.

The TLC procedure is carried out as follows. Use commercially available TLC sheets coated with silica gel and containing a fluorescent indicator. A portion of a sheet measuring 100 mm × 30 mm is adequate. Spot aliquots of volume 1 µl of several fractions adjacent to each other approximately 15 mm from the bottom of the sheet and place the sheet in a small jar containing methanol 10 mm deep. Cover the jar and allow the

methanol to climb up the sheet to 5 mm from the top. Remove the sheet and allow the methanol saturating the sheet to evaporate. MAP produces a dark spot when viewed under short wavelength UV light which glows under irradiation with long wavelength UV. Identify the MAP spot by comparing the retention factor, R_f, of the aliquot spots with the R_f of a MAP standard.

Based on TLC analyses, combine the fractions containing pure MAP. Weigh a round-bottomed flask to be used for rotary evaporation. Add the combined fractions to the flask, but do not exceed half the volume of the flask at any given time. Heat the evaporator bath to 35 °C to 40 °C and use water aspirator vacuum. After evaporation and trace solvent removal from all of the combined MAP fractions under high vacuum, weigh the flask and its contents to assess the yield.

Purify the MAP powder further by sublimation. Dissolve the MAP in a small volume of methylene chloride (< 20 ml) and transfer the solution to a sublimation apparatus. Allow the methylene chloride to evaporate under a gentle stream of nitrogen, keeping the MAP below the level of the bottom of the coldfinger. When the methylene chloride has evaporated, seal the vessel and reduce the pressure with a vacuum pump to 6,67 mPa[1)] or less. Begin a slow flow of cold water through the coldfinger and place the sublimation vessel in a wax bath maintained at 125 °C to 130 °C. Sublimation takes many hours and may need to continue overnight. Sublimation is complete when there is no further growth of MAP crystals on the coldfinger and the small amount of material remaining at the bottom of the apparatus appears constant. When complete, remove the crystals from the coldfinger with a spatula. A typical yield is 2,236 g (74 % mass fraction). The melting point of the MAP is 146 °C to 147 °C. The purity of MAP as assessed by HPLC is typically 99 % mass fraction.



Key

1 9-(chloromethyl)anthracene
2 piperazine
3 MAP

Figure 2 — Preparation of MAP

4.2 Reagent solutions

4.2.1 Impinger solution

Butyl benzoate, 99 % mass fraction, is used as the impinger solvent. The butyl benzoate is further purified by passing it through a bed of chromatography-grade silica gel. Dissolve MAP in the butyl benzoate to make a 1×10^{-4} mol/l solution (27,6 mg/l). Store the solution in a refrigerator until use.

1) 1 Pa = 7,5 torr.

4.2.2 Solution for filter impregnation

MAP is dissolved in acetonitrile to make a solution of 2 mg/ml. Store in a freezer until use.

4.2.3 Filter extraction solution

MAP is dissolved in acetonitrile to make a 1×10^{-4} mol/l solution (27,6 mg/l). Store in a freezer until use.

4.2.4 Stability of reagent solutions

It is best to make filter-spiking solution immediately before use, but this solution can be stored for up to 2 weeks in a freezer. The impinger and filter extraction solutions are stable for at least 1 month in a refrigerator.

4.3 Standard matching solutions

The UV detector response is nearly identical for all MAP-derivatised isocyanate groups. This allows the use of the MAP-derivatised monomer of the isocyanate product of interest as a standard for quantification of the other unknown oligomeric MAP-derivatised species in the chromatogram. A calibration curve, plotting UV response as a function of number or concentration of isocyanate groups, can then be used to quantify the oligomeric species for which there is no standard available. For this reason, it is conceptually simpler to use standard matching solutions quantified in terms of their concentration of isocyanate groups rather than in terms of mass concentration of isocyanate compound.

An equivalent is the amount of substance of isocyanate compound containing a mole of isocyanate group or the amount of substance of MAP-derivatised isocyanate compound containing a mole of bound MAP groups. The equivalent mass of an isocyanate compound is the relative molecular mass divided by the number of isocyanate groups per molecule, n. The equivalent mass of a MAP-derivatised isocyanate compound is the relative molecular mass divided by the number of MAP groups per molecule. The number of isocyanate groups, irrespective of their attachment, can be measured in moles per litre. Table 1 lists relative molecular masses and equivalent masses for common isocyanates and their MAP derivatives.

4.3.1 Preparation of monomer derivatives

Accurately weigh approximately 0,5 mmol (1 milliequivalent) of diisocyanate or 1 mmol (1 milliequivalent) of a monoisocyanate and record the amount of substance to four decimal places. Dissolve in 10 ml of toluene. Weigh approximately 1,2 mmol of MAP (20 % mass fraction excess) and record the amount of substance to four decimal places. Dissolve in 20 ml of toluene. While stirring the MAP solution, add the isocyanate solution dropwise over a period of 10 min to 15 min. Continue to stir for at least 1 h. Tightly cover the solution and store overnight in a freezer to maximise precipitation of product. Collect the precipitate using a Büchner funnel. Wash the precipitate several times with cold toluene to remove residual MAP, then wash it several times with cold hexane to displace the toluene. Transfer the solid derivative to a preweighed 20 ml disposable vial. Subject the vial to high vacuum until constant mass is obtained and seal with a PTFE-lined cap. Yields are typically > 95 % mass fraction and purity is sufficient to use this material for standard matching solutions. Experience shows that when stored in the dark in a freezer, these derivatives are stable for several years.

4.3.2 Preparation of standard solutions of monomer derivatives for HPLC analysis

Of a MAP derivative, weigh approximately $5,0 \times 10^{-5}$ mol (monoisocyanate) or $2,5 \times 10^{-5}$ mol (diisocyanate) ($5,0 \times 10^{-5}$ equivalents) into a 10 ml one-mark volumetric flask, ISO 1042[1], class A. Dissolve in several millilitres dimethyl formamide (DMF) and fill to the mark with DMF. Methylene chloride can be used instead, if desired, for MAP derivatives that are very soluble in methylene chloride (aliphatic diisocyanates and 2,4-TDI). The stock solutions are of approximate concentration $5,0 \times 10^{-3}$ mol/l (monoisocyanate) or $2,5 \times 10^{-3}$ mol (diisocyanate). Store the stock solutions in a freezer. Working standards are made by dilution into acetonitrile, with the highest concentration standard being approximately $2,0 \times 10^{-4}$ mol/l (monoisocyanate) or $1,0 \times 10^{-4}$ mol/l (diisocyanate). Other concentrations can be made by serial dilution, typically the lowest concentration being approximately 1×10^{-7} mol/l (monoisocyanate) or $0,5 \times 10^{-7}$ mol/l (diisocyanate). These stock solutions and dilutions are stable for up to 3 months when stored in a refrigerator.

Table 1 — Relative molecular masses and equivalent masses of some common isocyanates and their MAP derivatives

Compound	Short form	Relative molecular mass	Equivalent mass m[eq]	MAP derivative relative molecular mass	MAP derivative equivalent mass
1-(9-Anthracenylmethyl)piperazine	MAP	276,38	276,38	—	—
Methyl isocyanate		57,05	57,05	333,43	333,43
Butyl isocyanate		99,13	99,13	375,51	375,51
Phenyl isocyanate		119,12	119,12	395,50	395,50
1,6-Hexamethylene diisocyanate 1,6-diisocyanatohexane	HDI	168,20	84,10	720,96	360,48
Toluene diisocyanate (both 2,4- and 2,6-diisocyanatotoluene)	TDI	174,16	87,08	726,92	363,46
Isophorone diisocyanate 1-isocyanato-3-isocyanatomethyl-3,5,5-trimethylcyclohexane	IPDI	222,29	111,14	775,05	387,52
4,4'-Diphenylmethane diisocyanate Di-(4-isocyanatophenyl)methane	4,4'-MDI	250,26	125,13	803,02	401,51
Hydrogenated MDI Methylenebis(cyclohexyl-4-isocyanate) 4,4'-Dicyclohexylmethane diisocyanate	HMDI	262,35	131,18	815,11	407,56
Isocyanate group	NCO	42	42	—	—

4.3.3 Preparation of standard solutions of monomer derivatives for solid-phase extraction (SPE)

Evaluate recovery of MAP-derivatised monomers through solid-phase extraction (SPE) cartridges periodically.

Stock solutions in DMF cannot be used to make SPE standards because even low concentrations of DMF appear to cause premature elution of MAP derivatives. Standards to be passed through an SPE cartridge should be derived from methylene chloride stock solutions. MAP-derivatives of aliphatic diisocyanates and 2,4-TDI are quite soluble in methylene chloride. MAP derivatives of 2,6-TDI and MDI are less soluble. All MAP-derivatives except the MAP derivative of MDI are sufficiently soluble to prepare 1×10^{-3} mol/l (monoisocyanate) or $0{,}5 \times 10^{-3}$ mol/l (diisocyanate) stock solutions. A stock solution of concentration 2×10^{-4} mol/l can be made for the MAP derivative of MDI. These stock solutions can be further diluted into butyl benzoate to simulate impinger solutions.

4.3.4 Preparation of derivative solutions of bulk isocyanate products

This procedure has been found to be suitable for HDI- and IPDI-based products, and may be suitable for other products as well.

Weigh approximately 0.5 g of bulk isocyanate product into a 7 ml vial. Then add 4,5 g (3,4 ml) methylene chloride to this, and mix until the solution is homogeneous. Determine the density of this stock solution, unless subsequent analyses are for qualitative purposes only. Dilute the stock solution 1 → 100 (10 µl → 1 ml) in methylene chloride. Mix until the solution is homogeneous, then immediately add 25 µl of this dilution to 975 µl of 5×10^{-4} mol/l MAP in acetonitrile. It is important to make this second dilution into the derivatising solution as quickly as possible because dilute solutions of free isocyanates are not stable. Allow this final solution to react overnight in the dark. The next day, add 5 µl of acetic anhydride and allow to react at least 2 h at room temperature or overnight in a refrigerator before analysing by HPLC.