
**Determination of organonitrogen
compounds in air using liquid
chromatography and mass
spectrometry —**

Part 1:

**Isocyanates using dibutylamine
derivatives**

iTeh STANDARD PREVIEW
(standards.iteh.ai)

*Détermination des composés organiques azotés dans l'air par
chromatographie liquide et spectrométrie de masse —*

<https://standards.iteh.ai/catalog/standards/sist/2dc3723c-e314-4239-935f-9221007366719-17734-1-2006>

Partie 1. Isocyanates par les dérivés de la dibutylamine



PDF disclaimer

This PDF file may contain embedded typefaces. In accordance with Adobe's licensing policy, this file may be printed or viewed but shall not be edited unless the typefaces which are embedded are licensed to and installed on the computer performing the editing. In downloading this file, parties accept therein the responsibility of not infringing Adobe's licensing policy. The ISO Central Secretariat accepts no liability in this area.

Adobe is a trademark of Adobe Systems Incorporated.

Details of the software products used to create this PDF file can be found in the General Info relative to the file; the PDF-creation parameters were optimized for printing. Every care has been taken to ensure that the file is suitable for use by ISO member bodies. In the unlikely event that a problem relating to it is found, please inform the Central Secretariat at the address given below.

iTeh STANDARD PREVIEW
(standards.iteh.ai)

[ISO 17734-1:2006](#)

<https://standards.iteh.ai/catalog/standards/sist/2dc3723c-e314-4239-935f-92210b756b84/iso-17734-1-2006>

© ISO 2006

All rights reserved. Unless otherwise specified, no part of this publication may be reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying and microfilm, without permission in writing from either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

Published in Switzerland

Contents

Page

Foreword.....	iv
Introduction	v
1 Scope	1
2 Normative references	1
3 Principle.....	1
4 Reagents and materials	3
5 Preparation of standard solutions	3
5.1 Reference compounds	3
5.2 Di- <i>n</i> -butylamine (DBA) derivatives of isocyanates	4
5.3 DBA derivatives of bulk isocyanates.....	5
5.4 DBA derivatives of isocyanates in thermal decomposition products of polyurethane (PUR) or urea-based resins	6
5.5 Stability.....	6
6 Apparatus	6
7 Air sampling	9
7.1 Pre-sampling laboratory preparation.....	9
7.2 Pre-sampling field preparations.....	9
7.3 Collection of air samples	9
7.4 Blanks	10
7.5 Raw material.....	11
7.6 Shipment of samples.....	11
8 Laboratory sample preparation.....	11
8.1 Sample sequence.....	11
8.2 Work-up procedure.....	11
9 Instrumental settings.....	12
9.1 HPLC program (LC-MS).....	12
9.2 HPLC program (LC-chemiluminescent nitrogen detector) (LC-CLND)	12
9.3 Mass spectrometer	12
10 Data handling	12
10.1 Identification.....	12
10.2 Calibration curves.....	13
10.3 Quantification	13
11 Interferences	13
12 Determination of performance characteristics	13
12.1 Introduction	13
12.2 Relevant uncertainty contributions and criteria.....	14
12.3 Assessment of performance characteristics, following the detailed approach in Reference [18]	14
Annex A (informative) Performance characteristics.....	22
Annex B (informative) Examples	24
Bibliography	28

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

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.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 17734-1 was prepared by Technical Committee ISO/TC 146, *Air Quality*, Subcommittee SC 2, *Workplace Atmospheres*.

ISO 17734 consists of the following parts, under the general title *Determination of organonitrogen compounds in air using liquid chromatography and mass spectrometry*:

- Part 1: *Isocyanates using dibutylamine derivatives*
- Part 2: *Amines and aminoisocyanates using dibutylamine and ethyl chloroformate derivatives*

Introduction

Isocyanates have been used in industry for about 50 years. They are commercially important chemicals mainly used for the production of polyurethane (PUR). In spite of controls to limit exposures, there are adverse health effects such as asthma, contact dermatitis and hypersensitivity pneumonitis as a consequence of exposure to isocyanates in some industrial sectors.

The analytical method for the determination of isocyanates in workplace air must be sensitive due to the high irritation and sensitization properties of isocyanates. Extremely low occupational exposure limits (OELs) exist in many countries, and concentrations well below the OEL ($< 1/100$) often must be determined. Isocyanates are very reactive and therefore cannot be analysed directly. Derivatization during sampling is required in order to prevent interfering reactions. Hundreds of different isocyanates are used in industry, and many more are formed during thermal degradation of PUR. Therefore the analytical method must be highly selective.

The determination of isocyanates in the work environment using di-*n*-butylamine (DBA) as a reagent and liquid chromatography-mass spectrometric detection (LC-MS) has been demonstrated to be a robust method. The development of the method was initiated when difficulties using the “older” methods during sampling of isocyanates in complex atmospheres were encountered (e.g. thermal decomposition of PUR) [1], [2], [3]. The reaction rate between DBA and isocyanates was found to be fast, and high concentrations can be used to secure instantaneous reactions and eliminate problems with interfering compounds [4], [5]. Using impinger flasks containing a reagent solution and a filter in series efficiently collects and derivatizes isocyanates in both the gas and the particle phase [6]. LC-MS/MS of the isocyanate-DBA derivatives enables highly selective and precise determinations down to levels below 10^{-6} of the OEL [7].

Solvent-free sampling can also be performed by using a tube coated with a DBA-impregnated glass fibre filter followed by an impregnated filter. An impregnation solution containing DBA together with an acid is used, and the formed ion pair reduces volatility. DBA remains on the filter even after 8 h of sampling [8].

Monomeric isocyanates that are formed during thermal decomposition of polymers [typically PUR and phenol/formaldehyde/urea (PFU)-resins], such as isocyanic acid and methyl isocyanate, can also be determined [6], [7], [8], [9], [10]. Volatile isocyanate DBA derivatives can be determined using gas chromatography (GC)-MS [9]. Using the DBA-method and derivatization with ethyl chloroformate makes simultaneous determinations of amine, aminoisocyanates and isocyanates possible, as described in the companion method ISO 17734-2.

For quantification, reference compounds are necessary but are only available for a few monomeric isocyanates. Most of the isocyanates that are used in industry for the production of PUR can only be obtained in technical grade mixtures. Many isocyanates that are formed during thermal degradation are not available and are not easily synthesized. In this method, a nitrogen sensitive detector has been used for quantifying isocyanates in reference solutions. This technique has been demonstrated to be a useful tool, together with MS characterization, in greatly facilitating the production of reference solutions [10], [11], [12].

For quantifying isocyanates in complex mixtures, MS detection is necessary and provides a unique possibility of identifying unknown compounds. This method has enabled assessment of new areas for which exposure to isocyanates previously was not known and has identified new kinds of isocyanates in the work environment [6], [7], [8], [9], [10], [11], [12].

iTeh STANDARD PREVIEW
(standards.iteh.ai)

ISO 17734-1:2006

<https://standards.iteh.ai/catalog/standards/sist/2dc3723c-e314-4239-935f-92210b756b84/iso-17734-1-2006>

Determination of organonitrogen compounds in air using liquid chromatography and mass spectrometry —

Part 1: Isocyanates using dibutylamine derivatives

1 Scope

This part of ISO 17734 gives general guidance for the sampling and analysis of airborne isocyanates in workplace air. When amines and aminoisocyanates are suspected to be emitted (e.g. from thermal degradation of PUR), it is recommended that in addition to isocyanates the amines and aminoisocyanates in air are determined, using DBA and ethyl chloroformate as reagents (ISO 17734-2).

The method is suitable for the determination of a wide range of different isocyanates in both the gas and particle phases. Typical monofunctional isocyanates that can be determined are isocyanic acid (ICA), methyl isocyanate (MIC), ethyl isocyanate (EIC), propyl isocyanate (PIC), butyl isocyanate (BIC), and phenyl isocyanate (PhI). Typical monomeric diisocyanates include 1,6-hexamethylene- (HDI), 2,4- and 2,6-toluene- (TDI), 4,4'-diphenylmethane- (MDI), 1,5-naphthyl- (NDI), isophorone- (IPDI), and 4,4'-dicyclohexylmethane diisocyanate (HMDI). Multifunctional isocyanates that can be determined are typically oligomers in polymeric MDI, biuret-, isocyanurate-, and allophanate-adducts and prepolymeric forms of isocyanates.

The instrumental detection limit for aliphatic isocyanates is about 50 fmol and for aromatic isocyanates, it is 2 fmol. For a 15-l air sample, this corresponds to 0,6 ng·m⁻³ for HDI and 0,02 ng·m⁻³ for TDI.

The useful range, for a 5-l air sample, of the method is approximately 0,001 µg·m⁻³ to 200 mg·m⁻³ for TDI.

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 16200-1:2001, *Workplace air quality — Sampling and analysis of volatile organic compounds by solvent desorption/gas chromatography — Part 1: Pumped sampling method*

ISO 5725-2:1994, *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* (including Technical Corrigendum 1:2002)

3 Principle

Samples are collected by drawing a known volume of air through a midjet impinger flask followed by a filter. The impinger contains 10 ml of 0,01 mol l⁻¹ of DBA in toluene and the filter is a glass fibre filter with no binder.

Solvent-free sampling can also be performed by drawing air through a tube coated with a DBA-impregnated glass fibre filter followed by an impregnated filter. An impregnation solution containing DBA together with acetic acid is used, the ion pair so formed reducing the volatility and enabling long-time sampling.

After sampling, deuterium-labelled DBA-isocyanate derivatives (used as internal standard) are added to the sample solutions. The excess reagent and solvent are evaporated, and the samples are dissolved in acetonitrile. The samples are analysed using reversed-phase LC and electrospray (ESP)-MS detection, monitoring positive ions. Quantification is made by monitoring selected ions. See Figure 1.

Quantification and qualitative determinations can be performed using different LC-MS or LC-MS/MS techniques. LC-CLND (chemiluminescent nitrogen detection) or for aromatic isocyanates LC-UV (ultraviolet detection) can be used for the determination of higher concentrations of isocyanates.

Reference materials can be characterized using LC-MS/CLND. For characterization of volatile compounds, GC-thermionic specific detector (TSD) can also be used.

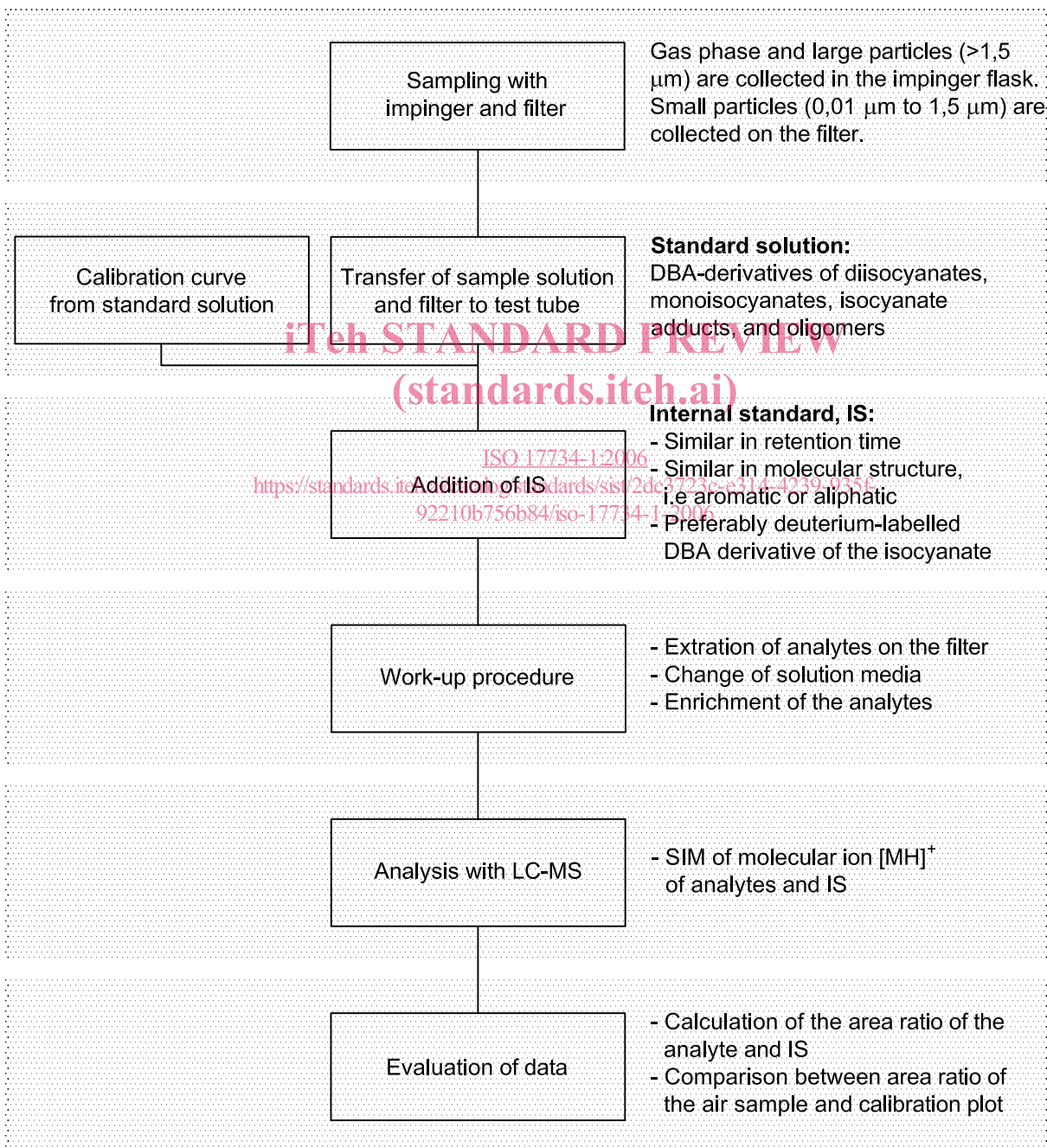


Figure 1 — Principle of the described method

4 Reagents and materials

4.1 DBA reagent.

Analytical grade di-*n*-butylamine is commercially available.

4.2 Solvents.

The reagent solvent, typically toluene, and other solvents, acetonitrile, isooctane and methanol, should be of liquid chromatographic quality.

4.3 Formic acid, concentrated formic acid, analytical grade.

4.4 Acetic acid, concentrated acetic acid, analytical grade.

4.5 Reagent solution.

In a 1-l volumetric flask, dilute 1,69 ml of DBA in toluene, and make up to the mark. The solution is stable and no special care during storage is necessary.

4.6 Reagent solution for solvent-free sampler.

4.6.1 Solution 1: 0,74 mol l⁻¹ DBA.

Mix 80 ml methanol and 12,5 ml DBA in a 100 ml volumetric flask. Then while stirring, slowly add 4,16 ml of acetic acid to the flask. Finally, add methanol to the flask, and make up to the mark.

4.6.2 Solution 2: 1,5 mol l⁻¹ DBA.

Mix 60 ml methanol and 25 ml DBA in a 100 ml volumetric flask. Then while stirring, slowly add 8,32 ml of acetic acid to the flask. Finally, add methanol to the flask, and make up to the mark.

4.7 HPLC mobile phases.

4.7.1 LC-MS.

The weak mobile phase (mobile phase A) consists of water/acetonitrile (95/5 volume fraction) and 0,05 % formic acid. The strong mobile phase (mobile phase B) consists of water/acetonitrile (5/95 volume fraction) and 0,05 % formic acid. The mobile phases are degassed prior to use.

4.7.2 LC-CLND.

The weak mobile phase (mobile phase C) consists of water/methanol (95/5 volume fraction) and 0,05 % formic acid. The strong mobile phase (mobile phase D) consists of water/methanol (5/95 volume fraction) and 0,05 % formic acid. The mobile phases are degassed prior to use.

5 Preparation of standard solutions

5.1 Reference compounds

Reference compounds are necessary for LC-MS determination of isocyanate derivatives. For the commercially available isocyanates, the DBA derivatives are easily prepared by direct derivatization with DBA. DBA derivatives for the isocyanates not commercially available can be made from the bulk material or from the thermal decomposition of PUR or urea-based resins used at the work place. Alternatively, standard solutions can be purchased.

5.2 Di-*n*-butylamine (DBA) derivatives of isocyanates

5.2.1 Preparation of isocyanate-DBA derivatives of commercially available isocyanates

Many frequently used isocyanates are commercially available from companies supplying laboratory chemicals such as HDI, 2,4- and 2,6-TDI, 4,4'-MDI, 4,4'-HMDI, 1,5-NDI, IPDI, PHI, MIC, EIC, PIC and BIC. The purity of the isocyanates varies, and some contain isomers.

Calibration standards are made by spiking accurately weighed amounts or volumes (ca 0,1 mmol) of isocyanates in 100 ml of isooctane. A 1-ml volume is added to 100 ml of toluene containing 0,01 mol·l⁻¹ of DBA (ca 0,01 μmol·ml⁻¹ of the DBA derivative).

Synthesis of derivatives:

- Dilute 6 mmol of isocyanate in 2 ml of isooctane, and dissolve 60 mmol of DBA in 20 ml of isooctane.
- Add the isocyanate solution to the DBA solution dropwise under continuous stirring.
- Evaporate the reaction mixture to dryness in a rotating evaporator, and dry the residue under vacuum to remove excess DBA.

It is also possible to prepare the isocyanate-DBA derivatives by collecting thermal degradation products of corresponding carbamate esters in an impinger flask containing DBA solution (as in 5.2.3.3).

5.2.2 Preparation of ICA and MIC-DBA

When urea is thermally degraded, isocyanic acid (ICA) is formed.

Heat an amount of urea (20 mg) to about 300 °C in a glass tube. Collect the degradation products in an impinger flask containing DBA in toluene (0,5 mol·l⁻¹). Wash the toluene solution containing the ICA-DBA derivatives with water, whereupon the organic phase is evaporated in a vacuum centrifuge and the residue is dissolved in methanol. Characterize the solution as described in 5.2.4.

The same procedure can be applied for preparation of MIC-DBA derivatives, by collecting thermal degradation products of 1,3-dimethyl urea.

5.2.3 Preparation of deuterium-labelled isocyanate-DBA derivatives

5.2.3.1 Internal standards

For accurate LC-MS quantifications, it is important to use proper internal standards, not only to compensate for variations during the work-up procedure, but also to compensate for fluctuation in the MS instrument response. Ideally, each analyte should have its own deuterium-labelled analogue. For isocyanate-DBA determinations, it is possible to use DBA derivatives of deuterium-labelled isocyanates or d₉- and d₁₈-DBA derivatives of the isocyanates as internal standards.

The quality of the quantification is influenced by the number of deuterium substitutions in the internal standard (less deuterium in the molecule resulting in higher precision). Having the deuterium on the isocyanate, and not on the DBA, has advantages when performing structural identification using MS and MS/MS. It is then possible to distinguish between labelled and non-labelled fragments that originate from the isocyanate itself. Therefore, the ideal internal standards are the DBA derivatives of the deuterium-labelled isocyanates. However, they are labour intensive to prepare, and they are only available for a few isocyanates.

The deuterium-labelled d₉- and d₁₈-DBA derivatives are easy to prepare, and any technical isocyanate or thermal degradation product can be derivatized and used as internal standard.

5.2.3.2 DBA derivatives of deuterium-labelled isocyanates

Dissolve a 10 mmol aliquot of the deuterium-labelled corresponding amine in 20 ml of toluene. Thereafter, add 150 μl pyridine and 40 ml of $5 \text{ mol}\cdot\text{l}^{-1}$ NaOH. Then add 1,5 ml of ethyl chloroformate dropwise under continuous stirring. After 10 min, the toluene phase is separated, and the solvent is evaporated.

Place the residue containing the formed amine carbamate ester (10 μl) in a glass tube. Heat the tube to about 300 °C. By connecting the tube to an impinger flask, containing $0,5 \text{ mol}\cdot\text{l}^{-1}$ DBA in toluene, the formed deuterium-labelled isocyanate is collected as a DBA derivative. Evaporate the solvent, and dissolve the residue in methanol to an appropriate concentration. Characterize the solution as described in 5.2.4.

5.2.3.3 d_9 -DBA and d_{18} -DBA derivatives of the isocyanates.

Prepare the deuterium-labelled d_9 - and d_{18} -DBA derivatives by dissolving accurately weighed amounts of the isocyanates in 10 ml of $0,1 \text{ mol}\cdot\text{l}^{-1}$ d_9 -DBA or d_{18} -DBA in toluene.

Prepare the deuterium-labelled derivatives of ICA and MIC by placing an amount (20 mg) of urea (for ICA) and 1,3-dimethyl urea (for MIC) in a glass tube. Heat the tube to about 300 °C and collect the formed ICA and MIC in impinger flasks containing $0,1 \text{ mol}\cdot\text{l}^{-1}$ d_9 -DBA or d_{18} -DBA in toluene. Evaporate the solutions containing the isocyanate d_9 -DBA or d_{18} -DBA derivatives to dryness, and dissolve the residues in methanol. Characterize the solution as described in 5.2.4.

5.2.4 Characterization

The solutions are diluted in methanol to appropriate concentrations and characterized on the LC-MS and quantified on the LC-CLND. This technique is nitrogen specific and any nitrogen-containing compound can be used as external standard, e.g. caffeine. The technique is used in several applications [13], [14], [15]. Quantification of volatile isocyanate-DBA derivatives can also be made by using GC-TSD.

5.3 DBA derivatives of bulk isocyanates

ISO 17734-1:2006
<https://standards.iteh.ai/catalog/standards/sist/2dc3723c-e314-4239-935f-92210b756b84/iso-17734-1-2006>

5.3.1 Preparation

Technical isocyanates used in industry are typically available in mixtures such as oligomers in polymeric MDI, biuret-, isocyanurate-, allophanate-adducts and prepolymeric forms of isocyanates. These isocyanates are typically multifunctional.

If product data sheets are available and correct, standard solutions for the technical grade isocyanates can be prepared in the same way as described in 5.2.1 by adding a known amount of bulk isocyanate to a toluene solution of DBA. If data regarding the composition and concentrations of different isocyanates are of poor quality or missing, the bulk material must to be characterized.

The procedure for technical grade isocyanate is as follows.

- Add an aliquot of 10 mg of the isocyanate product to a 10 ml vial containing $0,5 \text{ mol DBA}\cdot\text{l}^{-1}$.
- Sonicate the solution and evaporate it to dryness and then dissolve it in methanol.
- Further dilute the solution with methanol to appropriate concentrations.
- Characterize the solution as described in 5.3.2.

5.3.2 Characterization

If the isocyanates that are present in the bulk are known or reference compounds are available, calibration standards can be prepared as in 5.2.1.

If the isocyanates that are present in the bulk are unknown, qualitative data are obtained with full scan chromatograms for DBA derivatized bulk material. Obtained structural data together with the LC-CLND data make it possible to calculate the concentrations of the different components in the solution. The characterized bulk sample solution is used as a calibration standard for LC-MS.

When prepolymeric forms or complex isocyanates are to be determined, it may be difficult to quantify each individual isocyanate using LC-MS. However, one or more components can be used as index compounds. The total isocyanate group (NCO) concentration of the bulk is obtained by titration with DBA [16] and standard solutions can be prepared (dilution). The concentration of isocyanates in the air sample is estimated by comparison of peak areas. This may be performed with the assumption that the composition of the bulk material reflects the composition of the airborne isocyanates. The obtained result gives the concentration of total isocyanate content in the air. However, detection limits are increased by the factor of the ratio of total isocyanate concentration and the assumed concentration of the index isocyanate. Still, in most cases, levels below 1/10 of the threshold limit value (TLV) are possible to determine.

5.4 DBA derivatives of isocyanates in thermal decomposition products of polyurethane (PUR) or urea-based resins

5.4.1 Preparation

During the thermal decomposition of e.g. PUR or urea-based resins, isocyanates are formed that are not commercially available. PUR or urea-based material can be thermally decomposed at appropriate temperatures. Emitted degradation products are collected in impinger flasks (filters in series) containing 0,5 mol DBA·l⁻¹. The solutions are evaporated to dryness and the residues are dissolved in methanol.

5.4.2 Characterization

Qualitative data are obtained with LC-MS. Obtained structural data together with the LC-CLND data make it possible to calculate the concentrations of different components in the solution. The characterized diluted sample solution is used as a calibration standard for LC-MS.

iTeh STANDARD PREVIEW
(standards.iteh.ai)
ISO 17734-1:2006
<https://standards.iteh.ai/catalog/standards/sist/2dc3723c-e314-4239-935f-92210b756b84/iso-17734-1-2006>

5.5 Stability

Solutions of isocyanate-DBA derivatives (MDI, 2,4- and 2,6-TDI, HDI, IPDI, PhI, BIC, PIC, EIC, MIC and ICA) have been found stable in toluene, acetonitrile and methanol for six months when stored at 8 °C. NDI-DBA has limited stability and must be freshly prepared and quantified before using as a calibration standard.

6 Apparatus

6.1 Sampler.

Sample the air with an impinger flask followed by a filter.

6.1.1 Filter.

Use a 13-mm glass fibre filter (binder free) with a pore size of 0,3 µm.

6.1.2 Filter holder.

Use a 13-mm polypropylene filter holder with luer-lock connections.

6.1.3 Midget impingers.

A midget impinger consists of a tapered inlet tube. Match the two parts so that the distance between the inlet and the receiver bottom is 1 mm to 2 mm. A luer-lock fitting is attached to the outlet of the impinger.