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Sampling of diisocyanates (HDI, TDI) in air by derivatisation with secondary amines as reagents

Part 1. Partial rate factors (PRF) of reagents

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Relative differences in reactivity between reagents (all of which are secondary amines) particularly affect polyfunctional isocyanates, such as hexamethylene diisocyanate (HDI) and tolylene diisocyanate (TDI), compared with monoisocyanates. Thus, in 1994–1995, we carried out a programme of work to study the relative reactivity of the standard reagents, and of two alternative derivatising agents, by performing comparison tests on reaction rates. In the meantime, the reactivity of standard reagents used internationally for the determination of isocyanates in workplace atmospheres, as compared with some proposed “more reactive” alternative competitors, has been addressed by various authors. We measured the relative rates of reactions (partial rate factors) using the monomeric diisocyanates HDI and TDI and the monoisocyanate phenylisocyanate (PHI) separately in absorber solutions containing twin mixtures of different reagents. The partial rate factors of the reactions were found to vary by orders of magnitude using the diisocyanates HDI and TDI. They show a dependence on the chemical structure. Using the monoisocyanate PHI, our experimental results are consistent with literature data. Furthermore, our results clearly demonstrate that the proposed “most reactive” reagent dibutylamine (DBA) is less reactive towards HDI and TDI than is the reagent 1-(2-methoxyphenyl)piperazine (2-MP). In spite of the different reaction rates found, in our experience, up to now, there is “no-effect” on the analytical results when comparison tests are performed by monitoring isocyanates in air using DBA and the well known standard reagents. Work continues and results will be given in a following paper.

Introduction

The accuracy of the analytical determination of the real isocyanate concentration—free of artefacts—in workplace atmospheres may depend *inter alia* on the reaction rate of the reagent used. The knowledge of the relative reaction rates of reagents in relation to the isocyanate to be derivatised provides important information for the evaluation of analytical results. Besides the derivatisation of the isocyanate by the reagent, competitive reactions that lead to the formation of polyureas and/or polyurethanes may occur. The formation of the derivative therefore must be fast enough to render competitive reactions negligible.

Currently, only two publications[1,2] are known which relate to the measurement of the relative reactivities of reagents. These, as well as our tests, deal with the measurement of reaction rates of monoisocyanates in solution. The results cannot be transformed directly to air measurements without appropriate comparison tests. The different reactivities of the reagents affect the analytical results of air measurements if competing reactions interfere. However, water or alcohols react orders of magnitude more slowly with isocyanates than do amines. Differences in the relative reactivities of reagents become insignificant only if these compounds are taken into account as competing agents.

Monomeric diisocyanates are a class of chemical substances which have received a great deal of attention in recent years for a number of reasons. Compared with other compounds, they are very reactive towards functional groups such as $-NH_2$, $-NH$, $-SH$ or $-OH$. The air analysis of diisocyanates requires good experience with derivatisation techniques in order to obtain artefact-free “non-erroneous” results. Therefore, the analysis of isocyanates remains a subject for specialists. Local methods, where the essential difference is focused on the type of reagent used, have become established in the main industrial areas around the world. All methods are based on high pressure liquid chromatography (HPLC).[3] The choice of reagent used frequently depends on the particular country and on the history behind the development of the method. Since 1979, 4-nitrobenzylpropylamine[4] (nitro-reagent A), which was originally used to advantage in thin layer chromatography, has been the candidate in Germany. In the USA, 1-(2-pyridyl)-piperazine (2-PP) replaced the initially common nitro-reagent. In the UK, 1-(2-methoxyphenyl)-piperazine (2-MP) is now used. These reagents are the most important reagents used worldwide.

Besides their advantages, the different reagents also have individual disadvantages which become evident during routine analysis. The disadvantages may be: an insufficient shape of the component peak in HPLC caused by the high polarity of the derivative (reagents of piperazine type), poor solubility which is caused by the high molecular weight of the derivative urea (reagents of aminoanthracene type) and, unfavourable detection wavelengths in the UV (dibutylamine, DBA). Thus the development of reagents for isocyanate monitoring is an active area of research.

Recently, DBA has been the focus of attention in several publications.[5] This is associated with the belief that, due to its strong reactivity, DBA provides more reliable analytical results than the established standard reagents. It can be foreseen that the discussion about which is the best reagent will be dominated in the future by an analytical coupling technique which combines HPLC and mass spectrometric (MS) detection. This technique has been used increasingly in the last 2 years and is now available as an instrument for routine analysis. This is a part of an ongoing change that may have a lasting influence on the methodology of isocyanate analysis. In principle, any of the known reagents with good ion yields on spray ionisation can be used for this technique. Consequently, this will lead to more standardisation in methods with respect to the number of reagents needed. One essential requirement for monitoring isocyanates in workplace atmospheres is currently gaining importance, and that is the ability of the reagent to react sufficiently rapidly.

Reagent reactivities are measured under well-controlled steady state conditions. In field measurements, the reaction of a reagent is additionally influenced by, for example, catalytic effects, side reactions or solubilities. Therefore, the numerical power of partial rate factors is not so relevant in practice. During air sampling the reagents are always available in such a high excess that even the slowest of the commonly used reagents is not markedly affected by competing side reactions. The net result of the overall reaction between the reagent and the isocyanate must be taken into account.

The following section gives an overview of the theoretical and practical aspects of measuring relative reactivities in test solutions. In the experimental part of this paper, test results of the most frequently used amine reagents, as well as of two new reagents are described and evaluated.

Background and definitions of the relative rates of reaction

The relative difference in the reactivity of individual reagents with a known isocyanate substrate is expressed by the ratio *p* of the reaction rate constants, also called the partial rate factor (PRF):

$$p_{\mathrm{AB}} = \frac{k_{\mathrm{A}}}{k_{\mathrm{B}}} \qquad (1)$$

The PRF can easily be determined by simple competitive reaction tests without investigating the real order of the kinetics. However, this holds only in the case of an identical order of reaction. To measure *p*, a standard isocyanate is reacted with a mixture of two reagents, both of which are present in excess, in a known ratio. The parallel reactions in which urea derivatives are formed proceed as “pseudo-first-order” reactions with respect to the isocyanate group. Fig. 1 shows the concentration/time dependence for two possible urea derivatives of a monoisocyanate together with their initial gradients for an unknown order reaction. When isocyanate is added, the rate of reagent consumption is always proportional to the formation of the urea derivative at any time.

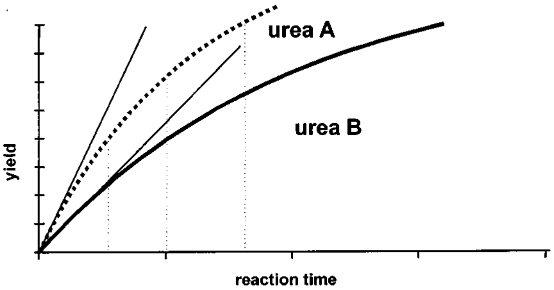

Fig. 1 Urea derivative formation as a function of reagent and reaction time for a monoisocyanate.

The following expressions[6] are derived from the basis of a “first-order” reaction, but the result will hold for parallel reactions of higher order also as long as they are of the same order.

For a given number of competitive reagents *N* in excess and an isocyanate *M* of amount *m* (*e.g.* a monoisocyanate such as phenylisocyanate), in the case of first-order reactions the conditions are: at the start of reaction: $t = 0$; $c_M = m$; at reaction time *t*: $t = t$; $c_M = m - x$.

In eqn. (2), the amount of isocyanate consumed is equal to the total amount of urea derivatives formed (U_{A}, U_{B}, ... U_N) at a reaction time *t*:

$$\begin{aligned} \frac{\mathrm{d}x}{\mathrm{d}t} &= k_{\mathrm{A}} \cdot (m-x) + k_{\mathrm{B}} \cdot (m-x) + \ldots + k_N \cdot (m-x) \\ \frac{\mathrm{d}x}{\mathrm{d}t} &= (k_{\mathrm{A}} + k_{\mathrm{B}} + \ldots + k_N) \cdot (m-x) \end{aligned} \qquad (2)$$

For $k_{\mathrm{A}} + k_{\mathrm{B}} + \ldots + k_N = k$, eqn. (2) can be rewritten as:

$$(m - x) = a \cdot \mathrm{e}^{-kt} \qquad (3)$$

For the calculation of the individual amounts of the ureas formed, *e.g.* urea A, U_{A}, the unknown *x* can be eliminated for the start of the reaction when $t = 0$; $U_{\mathrm{A}} = 0$ according to:

$$\frac{\mathrm{d}U_A}{\mathrm{d}t} = (m-x) \cdot k_{\mathrm{A}} = m \cdot k_{\mathrm{A}} \cdot \mathrm{e}^{-kt} \qquad (4)$$

The integration up to *t* and to U_{A} gives:

$$U_{\mathrm{A}} = \frac{m \cdot k_{\mathrm{A}}}{k} \cdot (1 - \mathrm{e}^{-kt}) \qquad (5)$$

The analogous calculations for the other urea products lead to eqns. (6) and (7):

$$U_{\mathrm{A}}/U_{\mathrm{B}}/\ldots/U_N = k_{\mathrm{A}}/k_{\mathrm{B}}/\ldots/k_N \qquad (6)$$

$$\frac{U_{\mathrm{A}}}{U_{\mathrm{B}}} = \frac{k_{\mathrm{A}}}{k_{\mathrm{B}}} = p_{\mathrm{AB}}, \ \textit{etc.} \qquad (7)$$

As a result of the derived kinetic equations for parallel reactions, the individual ratios of the urea derivatives are equivalent to the ratios of the corresponding reaction rates at any time. The (zero dimensional) ratios of the constants *k* are the required PRFs, the factors required to express the difference in reactivity of the reagents with respect to the tested isocyanate *M* [eqns. (1) and (7)].

In order to determine p_{AB}, it is sufficient to determine the ratio of the ureas at any point in the reaction, *i.e.* even after complete consumption of the added isocyanate. This provides urea concentration levels in the optimal working range of the analytical method. The procedure can be validated by multiple collection of samples from the reagent mixture at distinct time intervals while isocyanate addition is running or by repetitively performing the test with the reaction completed.

The instrumentation required to perform the comparison test is simply a vessel in which the two reagents to be compared are dissolved in known amounts. Their individual quantities must represent a molar excess with respect to the total amount of isocyanate to be added. The total amount of reagent must be virtually unchanged during the course of the reaction with the isocyanate. This procedure could also be applied to testing: (i) the effect of catalysts on the relative reactivity; (ii) the effect of masking components on the relative reactivity.

Relative rate constants in the case of polyfunctional agents

With regard to the equations derived above, only one reactive group in the isocyanate molecule has been considered, *i.e.* the equations apply to reactions of monofunctional partners. The ratio of the ureas which may be formed by bifunctional isocyanates (diisocyanates) in competitive reactions with two different monofunctional amines is proportional to the probability of the reaction. Weighted probabilities of reaction have to be considered here.

The distribution of reaction products (urea derivatives) obtainable is the result of a permutation over the available reactive centres. It can be described mathematically by the weighted binomial formula:

$$(p \cdot \mathrm{A} + \mathrm{B})^2 = p^2 \cdot \mathrm{A}^2 + 2p \cdot \mathrm{AB} + \mathrm{B}^2 \tag{8}$$

[p is a weighting factor for reagent component A, A and B are the reagent components, A^2 and B^2 are the ureas in which both isocyanate groups are derivatised by the same reagent ("pure" urea derivatives) and AB is the urea with differently derivatised isocyanate groups ("mixed" urea derivative)] when the isocyanate is a symmetrical diisocyanate, since only one mixed urea is formed, such as with HDI or 2,6-TDI (Fig. 2). Polyfunctional isocyanates with three or more isocyanate groups in the molecule are not considered in this article.

In the case of a bifunctional isocyanate, the three derivatives A^2, AB and B^2 occur in the molar ratios of $p^2/2p/1$. The weighting factor p is again the PRF. It is an average factor which does not take into account the effect of urea formation with the first substituent on the reactivity of the second substituent. Factor p can be calculated from the molar proportions of ureas formed with respect to the equimolar proportion of amines in the reagent solution in three different ways [{...} = molar proportion of]:

$$p_{\mathrm{AB}} = 0.5 \cdot \frac{\{\mathrm{AB}\}}{\{\mathrm{B}^2\}} \text{ or } p_{\mathrm{AB}} = 2 \cdot \frac{\{\mathrm{A}^2\}}{\{\mathrm{AB}\}} \tag{9a,b}$$

$$p_{\mathrm{AB}} = \sqrt{\frac{\{\mathrm{A}^2\}}{\{\mathrm{B}^2\}}} \tag{9c}$$

If the reactive groups are differentiated by reactivity (2,4-TDI in Fig. 2), eqn. (8) must be modified to take into account the different weightings of the substituent positions, which have different steric environments, to give:

$$(p_1 \cdot \mathrm{A}_1 + \mathrm{B}_1) \cdot (p_2 \cdot \mathrm{A}_2 + \mathrm{B}_2) = p_1 p_2 \cdot \mathrm{A}_1\mathrm{A}_2 + p_1 \cdot \mathrm{A}_1\mathrm{B}_2 + p_2 \cdot \mathrm{A}_2\mathrm{B}_1 + \mathrm{B}_1\mathrm{B}_2 \tag{10}$$

In this case, four urea derivatives occur in molar ratios of $p_1p_2/p_1/p_2/1$. In this normalised form, the coefficients p_1 and p_2 are the PRFs of the *ortho*- and *para*-located isocyanate groups and the ratio p_1/p_2 describes the relative difference in reactivity caused by the steric effects prevalent at the *ortho*- and *para*-located isocyanate groups.

The weighting factors are calculated as:

$$p_{\mathrm{oAB}} = \frac{\{\mathrm{A}_1\mathrm{A}_2\}}{\{\mathrm{A}_2\mathrm{B}_1\}} \text{ or } p_{\mathrm{oAB}} = \frac{\{\mathrm{A}_1\mathrm{B}_2\}}{\{\mathrm{B}_1\mathrm{B}_2\}} \tag{11a,b}$$

$$p_{\mathrm{oAB}} = \sqrt{\frac{\{\mathrm{A}_1\mathrm{A}_2\} \cdot \{\mathrm{A}_1\mathrm{B}_2\}}{\{\mathrm{A}_2\mathrm{B}_1\} \cdot \{\mathrm{B}_1\mathrm{B}_2\}}} \tag{11c}$$

$$p_{\mathrm{pAB}} = \frac{\{\mathrm{A}_1\mathrm{A}_2\}}{\{\mathrm{A}_1\mathrm{B}_2\}} \text{ or } p_{\mathrm{pAB}} = \frac{\{\mathrm{A}_2\mathrm{B}_1\}}{\{\mathrm{B}_1\mathrm{B}_2\}} \tag{11d,e}$$

$$p_{\mathrm{pAB}} \sqrt{\frac{\{\mathrm{A}_1\mathrm{A}_2\} \cdot \{\mathrm{A}_2\mathrm{B}_1\}}{\{\mathrm{A}_1\mathrm{B}_2\} \cdot \{\mathrm{B}_1\mathrm{B}_2\}}} \tag{11f}$$

The urea yields are determined analytically using HPLC analysis. In this normalised form the equation is not really suitable for practical application. Different ureas have different detector responses and thus will lead to different calibration factors.

The derived mathematical approach formulates the overall reaction probability as the product of the reaction probabilities of the distinguishable and independently reacting isocyanate groups of the "isocyanate" molecule [eqn. (12)]. The probability of reaction of isocyanate groups with reagent amines is linked to the composition of the reagent amine solution, and is therefore described as the sum of the individual probabilities [eqn. (13)]. A weighted binomial formula is the result, which includes eqns. (8) and (10) (see above) in an appropriate manner:

$$W_{\mathrm{tot}} = W_1 \cdot W_2 \cdot \ldots \cdot W_n = \prod_{i=1}^{n} W_i \tag{12}$$

$$W_i = \{X_m + \sum_{j=1}^{m-1} [w_i \cdot X_j]\} \tag{13}$$

where n is the number (position) of distinguishable intramolecular isocyanate groups, m is the number of competing reagent amines X_j and w is the partial probability of reaction (partial rate factor).

Eqns. (8) and (10) must be expanded when different molar proportions of reagents and different calibration factors are considered. In the case of negligible internal molecular interactions, the detector response of a "mixed" urea derivative AB is assumed to approximate to the average of the two "pure" urea derivatives. This is based on practical experience.

The formulae derived from eqns. (8) and (10) are of great practical importance and represent a specific set of equations from which the PRF can still be determined when one of the "pure" urea derivatives, A^2 or B^2, is below the analytical detection limit. For instance, when there are large reactivity differences, *i.e.* for weighting factors $p << 1$ (or $p >> 1$), the terms of the "mixed" urea derivatives AB decrease less strongly than the corresponding squared terms [p^2 in eqn. (8) or p_1p_2 in eqn. (10)] of the "pure" urea derivatives. Thus the relative rate constants can still be determined from the yields of at least two different ureas [see eqns. (9a,b), (11a,b) and (11d,e)]. If we consider eqn. (8), then, for a partial rate factor p of 32, the ratio between the "pure" urea derivative A^2 and the "mixed" urea derivative AB is present in an easily measurable ratio $p/2$ of 16, while the ratio between the "pure" urea derivative B^2 and the "pure" urea derivative A^2 is 1 : 1024 and would be barely detectable to a sufficient degree of accuracy.

New reagents for isocyanate analysis

High selectivity, stability and sensitivity to detection have hitherto been required of reagents. As these properties depend on the molecular structure, *i.e.* the functionality (type and effect of functional groups) and geometry (three-dimensional structure and size), the selection of an amine has been governed by the most important property (evaluated positively). Designer reagents may sometimes provide these properties better than classical reagents.

We have additionally studied appropriate aspects of two alternative amines of 'nitro-reagent' type, which we hoped would offer advantages for the analytical detection of diisocyanates in air: *N*-(4-nitrophenethyl)-*N*-(*n*-propyl)-amine and 1-(4-nitrophenyl)-piperazine.

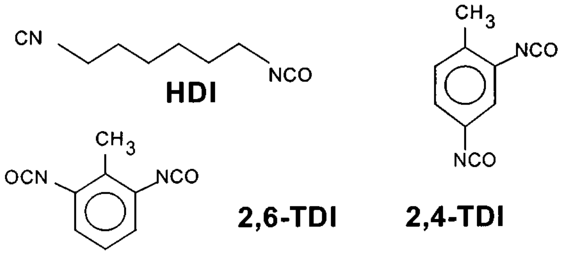

Fig. 2 Chemical structure of hexamethylene-1,6-diisocyanate (HDI), tolylene-2,6-diisocyanate (2,6-TDI) and tolylene-2,4-diisocyanate (2,4-TDI).

N-(4-Nitrophenethyl)-*N*-(*n*-propyl)-amine

N-(4-Nitrophenethyl)-*N*-(*n*-propyl)-amine (“nitro-reagent B”; “NR-B”) is a new derivatising agent for the detection of aliphatic and aromatic isocyanates in air. Due to better decoupling of the electron-deficient phenyl ring, this reagent should have improved reactivity as compared with *N*-(4-nitrobenzyl)-propylamine (“nitro-reagent A”; ”NR-A”), the classical nitro-reagent.

The compound was prepared using the procedure described for nitro-reagent A synthesis:[4] 0.06 mol (13.8 g) of β-(4-nitrophenyl)ethyl bromide (CAS 5339-26-4) was dissolved in 50 ml of toluene to which was added, dropwise, 0.18 mol (10.6 g) of *n*-propylamine in 10 ml of toluene under boiling reflux; the solution was then boiled for a further 4 h under reflux; after cooling the solution, the precipitated propylamine hydrobromide was removed by filtration under suction and washed with toluene; the filtrate was then concentrated using a rotary evaporator; 15 ml of water and 5 ml of concentrated caustic soda solution were then added to the residue and the mixture was shaken with 10 ml of toluene; the toluene extract was again concentrated and taken up in 10 ml of acetone; concentrated hydrochloric acid was added dropwise to this solution and the precipitated hydrochloride was separated by filtration under suction; the filter residue was then washed three times with 3 ml of a mixture of equal parts of acetone and toluene and dried in a vacuum drying cabinet for 24 h at 40 °C. The identity and purity of the free *N*-(4-nitrophenethyl)-*N*-(*n*-propyl)-amine were determined using NMR, MS (Fig. 3) and GC.

1-(4-Nitrophenyl)-piperazine

1-(4-Nitrophenyl)-piperazine (“nitro-reagent C”; “N-RC”) is a commercially available substance. It was used as an experimental derivatising reagent for detecting aliphatic and aromatic isocyanates in air. It is characterised, in addition to an absorption maximum at about 254 nm (Fig. 4), by an extremely long wavelength absorption band down to the visible region. The substance itself has an intense yellow colour and produces urea derivatives with an intense yellow colour. During HPLC analysis, a very good signal to noise ratio is achieved at the absorption maximum at about 375 nm because known components which could interfere, such as aromatic solvent components, show no measurable absorption at this wavelength. The molar absorption coefficient at the main absorption maximum is the largest among this group of reagents.

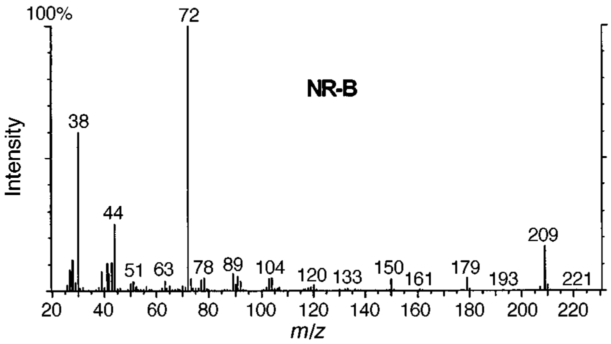

Fig. 3 Ion trap detector (ITD) mass spectrum of “nitro-reagent B”, *N*-(4-nitrophenethyl)-*N*-(*n*-propyl)-amine.

Chemicals

The chemicals used for the experimental trials were bought from chemical suppliers and optionally converted into the free bases.[4] They were not subjected to any particular purification taking into account the objective of the trials. The following synthesis components were used: β-(4-nitrophenyl)ethyl bromide (Merck, Darmstadt, Germany); *n*-propylamine (Merck). The following reference isocyanates (Fig. 2) were used: hexamethylene diisocyanate (HDI); 2,4-tolylene diisocyanate (2,4-TDI); phenylisocyanate (PHI). The following reagents (Fig. 5) were used: 1-(2-pyridyl)-piperazine (2-PP) (Aldrich, Steinheim, Germany); dibutylamine (DBA) (Merck); 1-(2-methoxyphenyl)-piperazine (2-MP) (Aldrich); nitro-reagent A (Merck); nitro-reagent B (synthesised); nitro-reagent C (Aldrich).

Fig. 5 shows the chemical structure of the tested reagents and Table 1 shows the absorption maxima and associated molar absorption coefficients of the ureas, which are formed by reaction of these reagents with HDI or TDI.

Experimental details relating to the competitive reaction measurements

In order to keep the test as simple as possible, equimolar solutions of the reagents to be compared were prepared separately in methylene chloride. The molar concentration was adjusted to a level which is employed in practice when taking air samples using wash bottles (about 0.01 M). The solution of the isocyanate component was freshly prepared in separately (molecular sieve) dried methylene chloride at an appropriate low molar concentration with respect to the number of isocyanate groups.

The calibration reaction was performed in separate batches of reagent solution in such a way that 1 ml of isocyanate solution was added to 100 ml of vigorously stirred reagent solution. The separate batches were then combined after this procedure. If bifunctional isocyanates are used, the separately reacted and subsequently combined solutions A and B contain the “pure”

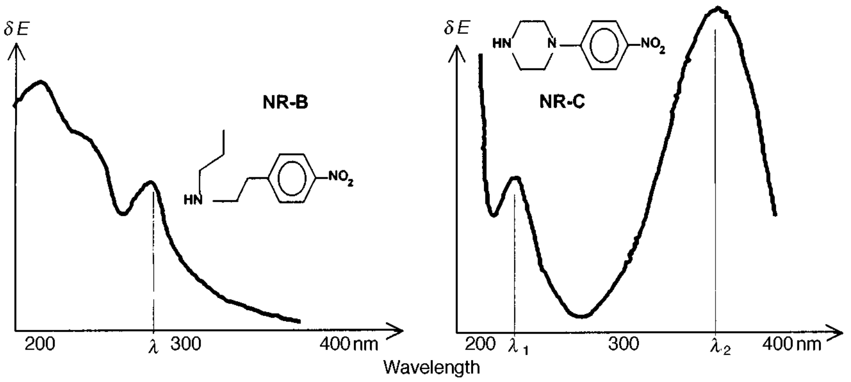

Fig. 4 UV absorption spectra of “nitro-reagent B” and “nitro-reagent C”.

urea derivatives in equimolar proportions, so that the response factor for urea derivative A^2 as compared with B^2 is obtained directly from the areas measured during HPLC analysis, in accordance with

$$f_{A^2B^2} = F_{A^2}/F_{B^2} \tag{14}$$

where $f_{A^2B^2}$ is the molar response factor between the "pure" urea derivatives.

The competitive reaction was performed in an equimolar mixture of reagents. The two reagent solutions A and B (50 ml of each) were combined and homogenised. Only then was 1 ml of isocyanate solution added to the vigorously stirred reagent mixture. Since only the "pure" urea derivatives are formed by preparing the calibration solution, solution "A + B" of the competitive reaction in the reagent mixture also contains "mixed" urea derivatives. The sum of the molar concentrations of the ureas is identical in both solutions. Both solutions were analysed under the same analytical conditions using HPLC with UV detection, which separates the two pure urea derivatives sufficiently selectively. The "mixed" urea derivatives appear between these two limiting points in the chromatogram in accordance with their "parentage". Fig. 6 shows examples of chromatograms for HDI and 2,4-TDI as isocyanate.

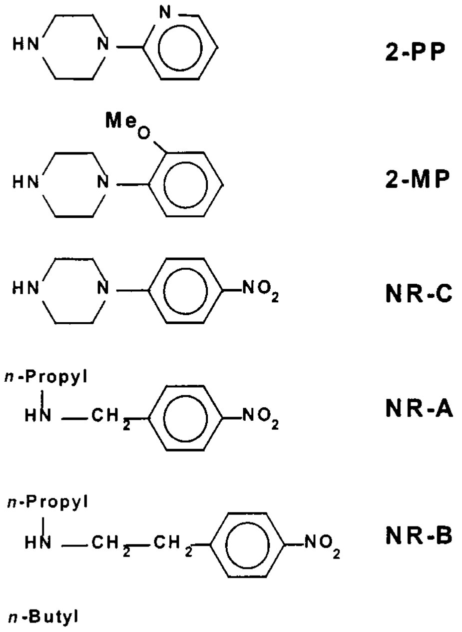

Fig. 5 Chemical structure of reagents.

Table 1 Absorption maxima λ_{max} (nm) and associated molar absorption coefficients ε (l mol^{-1} cm^{-1}) of urea derivatives[7]

	2,4-TDI		HDI	
Reagent	λ_{max}	ε	λ_{max}	ε
1-(2-Pyridyl)piperazine	252	60500	252	34700
1-(2-Methoxyphenyl)piperazine	247	42100	255	20000
N-(4-Nitrobenzyl)propylamine	248	31400	275	16600
N-(4-Nitrophenethyl)propylamine	255	30000	280	15000
1-(4-Nitrophenyl)piperazine	254	30000	254	20000
	370[a]	65000	370[a]	42000
Dibutylamine	254	15000	—	—

[a] Working wavelength: the absorption maximum is shifted, depending on the type of substituent in the urea derivative, and is higher than 370 nm. This wavelength is selected for practical considerations because it is in the range emitted by a deuterium lamp. Thus detection can be performed simultaneously in the main absorption region of the aromatic ring (about 254 nm) and in the region of the reagent chromophore.

HPLC run parameters for nitro-reagent C

The following HPLC parameters were used: equipment, HP 1090 1 DAD (Hewlett Packard, Waldbronn, Germany); column, Lichrosorb RP 18 (Merck), l = 250 mm, id = 4 mm; flow rate, 1.5 ml min^{-1}; oven temperature, room temperature; volume injected, 5 μl; detection 254 and 375 nm (UV); elution time 20 min. The composition of the eluent was as follows: solution 1 tetrahydrofuran; solution 2 1000 ml doubly distilled water, 10 ml triethylamine with phosphoric acid adjusted to pH 5.0. The following gradient programme (linear) was used: *t*0, 80% solution 2; *t*20, 20% solution 2; post time, 5 min (final condition).

The HPLC conditions were chosen in accordance with recognised literature methods.[4,8,9] They were individually adapted to the particular separating problem and not specified separately, with the exception of nitro-reagent C. Here the analytical conditions had to be modified so that all the derivatives could be sufficiently well separated. Since nitro-reagent C has two absorption maxima, components could be detected at 370 nm and at 254 nm in the UV region. Examples of simultaneously recorded chromatograms are given in Fig. 6.

Results

To calculate the PRFs, the normalised peak areas of HPLC analyses were determined using the response factors as described above. In accordance with the number of independent calculation formulae [eqns. (9) and (11)], the PRFs were determined, the average values found and the mathematical fit calculated using the basic formulae [eqns. (8) and (10)]. The PRFs were determined using the "mixed" urea derivatives in cases where a "pure" urea derivative was below the detection limit (see bottom chromatogram of Fig. 6).

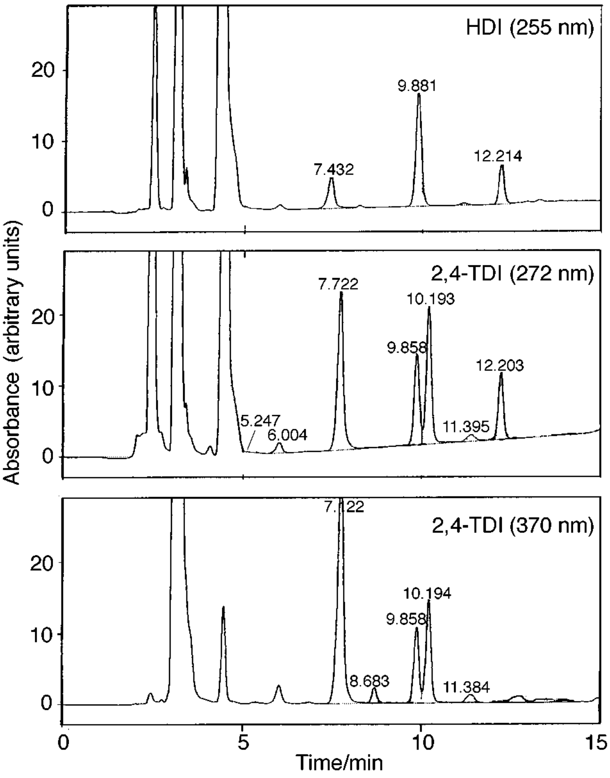

Fig. 6 HPLC chromatograms of ureas in a reaction mixture of nitro-reagent C *versus* nitro-reagent A with HDI at 255 nm (top) and 2,4-TDI at 272 nm (middle) and 370 nm (bottom) detected simultaneously.

The problem in determining the PRFs for reagents with large differences in reactivity was solved by using the slower reacting reagent in a 10-fold excess as compared with the competitive reagent (HDI example). Although the experimental time is doubled using this procedure, since a preliminary trial is required, the accuracy of the determination can be considerably increased.

Table 2 (left columns) shows the calculated PRFs (rounded) of all the tests performed with different pairs of reagents with HDI and 2,4-TDI. The bold values were determined experimentally. These matrix tables are entirely redundant, since rows and columns are in principle linearly dependent. Therefore some of the experimentally determined PRFs are indirectly available from calculations on the basis of the PRFs of other pairs of reagents. No correction was made. The italic PRFs were calculated because the ratios of values in a column were known, as was at least one value. The opportunity for reagents to react is doubled for diisocyanate molecules. Therefore the partial rates of reaction are expressed exponentially by the partial rate squared factors p^2 (PRSFs) according to the dependent probabilities of reaction. As before, the calculated PRSFs for HDI and TDI are given as matrix tables in Table 2 (right columns). The exponential effect in the PRSFs shows that moderate differences in relative reactivity will lead to an enormous increase in the differentiation of reactivities as more isocyanate groups are involved in an isocyanate molecule.

Partial rate factors of reagents (including nitro-reagent B) for phenylisocyanate (PHI)

Our new nitro-reagent B was not available for the tests shown above. In order to test nitro-reagent B under standardised conditions for comparison reasons with all the important reagents, in particular DBA, we conducted an additional set of tests (Table 3) in 1995. Since DBA-urea provides no response with aliphatic isocyanates in a UV detector, phenylisocyanate (PHI) was used as the reference isocyanate. It was assumed that this monoisocyanate would have less steric effects on the reactivity of reagents as compared with diisocyanates. In the case of monoisocyanates, the PRF for one isocyanate group is identical to the relative rate of reaction.

From this set of tests with PHI, nitro-reagent B exhibited the hoped-for large increase in reactivity as compared with nitro-reagent A. Overall, a slight reactivity advantage of DBA compared with the other test reagents must be considered. The relative sequence of reactivities of reagents, which was established by the tests performed using diisocyanates, was confirmed. Satisfactory agreement was found between the PRFs of selected reagents for PHI (Table 4) with those of other authors.[1]

Table 2 Partial rate factors (PRFs) and partial rate squared factors (PRSFs) of reagents for HDI and 2,4-TDI.[a]

PRF					PRSF				
HDI	2-MP	NR-A	NR-C	DBA	HDI	2-MP	NR-A	NR-C	DBA
2-MP	1	**41**	**13.4**	*1.9*	2-MP	1	**1680**	**180**	*3.6*
NR-A	**0.024**	1	**0.39**	**0.046**	NR-A	**0.0006**	1	**0.15**	**0.002**
NR-C	**0.07**	**2,6**	1	*0.117*	NR-C	**0.005**	**6.8**	1	*0.014*
DBA	*0.54*	**22**	*8.6*	1	DBA	*0.29*	**485**	*74*	1
2,4-TDI	2-MP	NR-A	NR-C	DBA	2,4-TDI	2-MP	NR-A	NR-C	DBA
2-MP	1	**27.5**	**17**	*6.9*	2-MP	1	**760**	**290**	*48*
NR-A	**0.036**	1	**0.51**	0.25	NR-A	**0.0013**	1	**0.26**	**0.063**
NR-C	**0.06**	**1.96**	1	*0.5*	NR-C	**0.0036**	**3.85**	1	*0.25*
DBA	*0.14*	**4.0**	*2.0*	1	DBA	*0.02*	**16.0**	*4.0*	1

[a] Bold values, experimentally determined; italic values, calculated on the basis of row to column of NR-A data.

Table 3 Partial rate factors (PRF) of reagents for PHI. Bold values, experimentally determined; italic values, calculated on the basis of the row to column for DBA data.

PHI	2-MP	NR-A	NR-B	NR-C	PP	DBA
2-MP	1	*14.9*	*1.5*	*3.9*	*1.2*	**0.67**
NR-A	*0.07*	1	*0.1*	*0.26*	*0.08*	**0.045**
NR-B	*0.67*	*10*	1	*2.6*	*0.8*	**0.45**
NR-C	*0.26*	*3.8*	*0.38*	1	0.3	**0.17**
PP	*0.83*	*12.3*	*1.2*	*3.2*	1	**0.56**
DBA	**1.5**	**22**	**2.2**	**5.8**	**1.8**	1

Competitive reaction measurement test by air sampling

In order to validate the results of test solutions, air was sampled in a concentration range close to the German threshold limit value (MAK) for TDI in air (0.07 mg m^{-3}) using a reagent mixture of 2-MP and DBA (midget impinger, 1 l min^{-1}, 30 min). The PRF was determined by performing six independent samplings of the test atmosphere. During the course of this trial, which demonstrates a real life situation, we confirmed the more rapid reaction of 2-MP as compared with DBA once more. 2-MP reacted about 1.2 to 1.5 times faster than DBA (Table 5).

We interpret the result for 2-MP by assuming that a catalytic effect is possibly exerted here by the tertiary piperazine nitrogen. Nitro-reagent C is not suitable as a reagent, not only due to its weak reactivity but also its poor solubility. In the case of nitro-reagent A, the basicity of the secondary amino group is again weakened by the inductive effect of the electron-deficient phenyl ring and this is the reason for its lowest reactivity of the reagents tested. If the electron capture effect is blocked by introducing an additional methylene group between the nitrogen and the phenyl ring, as in the case of nitro-reagent B, then the reactivity increases greatly.

The reactivity differences between 2-MP, nitro-reagent B, 2-PP and DBA are no longer significant when taking into account the experimental variance. DBA is relatively volatile and therefore suitable only for taking samples in wash bottles. Compared with DBA, the reagents 2-MP, nitro-reagent B and

Table 4 Partial rate factors (PRFs) of selected reagents for PHI, comparison of PRF (column 1 of Table 3) with literature data (2-MP = 1)

PHI	Wu *et al.*[1]	p_{PHI}
2-MP	1	1
PP	0.49	0.83
NR-A	0.04	0.067
Water	<< 10E-7	—

Table 5 Competitive reaction measurement test by air sampling: PRSFs of 2-MP *versus* DBA derived from air samples of 2,4-TDI

	Relative molar yield of urea derivatives		
Sample no.	2-MP (A^2)	AB + BA	DBA (B^2)
I	1	1.97	0.72
II	1	1.92	0.66
III	1	1.82	0.61
IV	1	1,93	0.60
V	1	1.82	0.66
VI	1	1.46	0.63
Mean values		1.82	0.65
PRF	p	1.1	1.24
PRSF	p^2	1.21	1.54

2-PP have substantial advantages, being suitable for impregnating surfaces for chemisorption, *i.e*. for taking tube and filter samples; and can also be used for aliphatic isocyanates with UV detection.

It has been shown that the tests for determining the relative reactivities of reagents using industrial diisocyanates are easy to perform and provide valuable additional information on the kinetics. In our tests, the relative differences in reaction rates between the *ortho*- and *para*-located isocyanate groups of TDI could be determined. The isocyanate group in the *ortho* position is a factor $p = 1.42 \pm 0.07$ less reactive than that in the *para* position. A comparable difference in reactivity should be observed if 2,4-TDI and 2,6-TDI are compared.

The experimental results show that the reactivity data from model tests with monoisocyanates cannot be readily transferred to diisocyanates. Differences in the relative reactivity of the reagents were observed between HDI and TDI. How far these were due to inherent errors of the test method or analytical method or the influence of steric effects was not further investigated (as mentioned previously, the competitive reaction of DBA and an aromatic reagent amine using HDI was only determined via the "mixed" urea derivatives which contain the aromatic chromophore of the reagent).

Conclusions

Competitive kinetic tests of the derivatising reaction of isocyanates with reagents of the secondary amine type show significant variations in reaction rates under laboratory conditions. The dependence of the partial rates of reaction on the type of isocyanate is not very pronounced. Nitro-reagent A reacted the most slowly and 2-MP the most rapidly. Nitro-reagent C appears to be unsuitable for air analysis. The observed reactivity of nitro-reagent B fits the theoretical expectation based on its chemical structure. However, the relative reaction differences between the reagent amines 2-MP, nitro-reagent B, 2-PP and DBA are not as obvious when experimental variations are taken into account. The relative reactivities of amine type reagents do not seem to be an essential prerequisite in field measurements, due to the high excess of reagent used for air sampling.

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