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Indirect determination of isocyanates by gas chromatography

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ABSTRACT

A gas chromatographic method was developed to determine the purity of synthesized isocyanate monomers, specifically isocyanatoacrylates, and to determine the isocyanate content of synthesized polymers and prepolymers. The method is a modification of an ASTM procedure in which an isocyanate is allowed to react with excess di-*n*-butylamine. In the ASTM method, the amount of isocyanate present is calculated indirectly from the amount of unreacted di-*n*-butylamine, determined by back titration with standard hydrochloric acid. Determination of the excess di-*n*-butylamine by the gas chromatographic method developed has the advantages of providing better precision and requiring less sample than the titrimetric method. The two methods were compared using phenyl isocyanate as a model test compound. A synthesized monomer, methyl α-isocyanatoacrylate, was also analyzed, for comparison by both methods.

INTRODUCTION

Several isocyanatoacrylate monomers are being synthesized and evaluated under an NIDR grant: "Development of new multifunctional dental adhesive, DE08223". These include the α and β isomers of methyl, ethyl, and hexyl isocyanatoacrylate. Prepolymers and copolymers of these monomers contain active isocyanate groups which will react with the hydroxyl and amino functional groups in tooth and composite materials to form covalent chemical bonds. Accurate information on the isocyanate content of the synthesized monomers and polymers is required for this work.

Current analytical methods are limited by high sample consumption requirements and/or by specificity of the methods, requiring modifications for each different compound of interest. These methods can be classified as direct or indirect. Direct methods measure isocyanate content from detector response to the isocyanate compound or its derivative. Indirect methods generally react the isocyanate with excess di-*n*-butylamine (*n*-DBA). The isocyanate content is calculated after quantitating the detector response to the unreacted *n*-DBA. The work reported here involves development of an indirect gas chromatographic method which provides precise

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quantitation for isocyanate content while not requiring large sample consumption or compound-specific parameters.

The literature on isocyanates and their reactions spans many years. Various analytical techniques have been utilized for quantitation. In addition to the ASTM method [1] cited, these techniques include spectroscopic methods such as IR [2–4] and UV [5], and chromatographic methods such as gas chromatography (GC) and high-performance liquid chromatography (HPLC). Although a few reported GC methods involve direct injection and detection of isocyanates [6,7], most involve some form of derivatization. After hydrolysis of isocyanates to amines and subsequent derivatization, usually with perfluoro fatty acid anhydrides [8–12], the corresponding amides can be detected. Other methods involve detection of the corresponding amines after hydrolysis [13] or detection of the corresponding urethanes after reaction with ethanol [14,15]. Various detection modes have been utilized. These include flame ionization (FID), nitrogen-specific (NPD) and electron-capture (ECD) detection.

Some reported HPLC methods involve derivatization of isocyanates with amines for detection of the resulting ureas with UV [16,17], fluorescence [18,19], or electrochemical [20] detectors. Aromatic isocyanates can be reacted with ethanol prior to HPLC analysis and detected as the corresponding urethanes either by UV or electrochemically [21–23]. Wong and Frisch [24] determined concentrations of unreacted phenyl isocyanate during kinetic studies of the reaction between phenyl isocyanate and *n*-butanol, by allowing the excess to react with *n*-DBA. Sample aliquots were quenched with *n*-DBA solutions and the amount of phenyl isocyanate calculated indirectly from the amount of unreacted *n*-DBA determined by back titration. Wong and Frisch also performed HPLC analyses to detect the reaction product, di-*n*-phenylbutyl urea, as well as initial and intermediate products.

EXPERIMENTAL

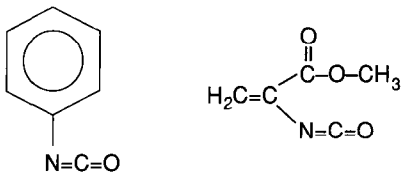
Reagents

Phenyl isocyanate and dodecane were obtained from Aldrich (Milwaukee, WI, U.S.A.). *n*-DBA was obtained from Eastman Kodak (Rochester, NY, U.S.A.). Toluene was obtained from Burdick and Jackson (Muskegon, MI, U.S.A.) and was certified to contain not more than 0.005% water. Isopropanol was obtained from Fisher Scientific (Fair Lawn, NJ, U.S.A.). Bromphenol blue indicator was prepared by mixing 0.100 g of bromphenol blue, obtained from Fisher Scientific, with 1.5 ml of 0.1 *M* sodium hydroxide solution and diluting to 100 ml with deionized water. Hydrochloric acid solution, 0.1 *M*, was obtained as Dilut-IT from Baker (Phillipsburg, NJ, U.S.A.) and was prepared with deionized water as per package directions. Methyl α-isocyanatoacrylate was synthesized at Midwest Research Institute.

Titration procedure

The ASTM method [1] was utilized. This method covers the determination of the isocyanate group content of a urethane intermediate or prepolymer. Possible interferences include phosgene, the carbamyl chloride of isocyanate, hydrogen chloride, or any other acidic or basic impurities of sufficient strength.

Replicate samples (at least five) of phenyl isocyanate or synthesized methyl α-isocyanatoacrylate (Fig. 1), 1.1 mequiv., were accurately weighed into 250-ml



A B

Fig. 1. Structures of (A) phenyl isocyanate and (B) methyl α-isocyanatoacrylate.

erlenmeyer flasks. Toluene, 25 ml, was added to each flask, which was then stoppered and swirled to mix. Using a pipet, 25 ml of a 0.1 *M* di-*n*-butylamine solution in toluene was added to each flask. The solutions were magnetically stirred for 30 min with stoppers in place. Isopropanol, 100 ml, was added to each. Five drops of the bromphenol blue indicator was added, and each sample was titrated with the 0.1 N hydrochloric acid to a yellow end point. Blank titrations were run including all reagents but omitting the isocyanate sample compound.

The isocyanate (NCO) content was calculated as follows:

$$\text{NCO}, \% = \{[(B - V) \cdot M \cdot 0.0420]/W\} \cdot 100$$

where B = milliliters of HCl required to titrate the blank, V = milliliters of HCl required to titrate the sample, M = molarity of HCl (0.1000), 0.0420 = milliequivalent weight of the NCO group, W = weight of sample in grams.

Gas chromatography procedure

The GC method developed is a modification of the ASTM procedure in that the isocyanate compound is allowed to react with excess *n*-DBA, but the amount of unreacted *n*-DBA is determined by GC analysis rather than by titration. An internal standard was added to correct for any volumetric and injection errors.

GC apparatus and operating conditions

A Varian Model 3700 gas chromatograph (Varian Instruments, Sunnyvale, CA, U.S.A.) equipped with a flame ionization detector and Model 8000 autosampler was used. The injector temperature was 300°C and the detector temperature was 320°C; the nitrogen carrier gas flow-rate was 70 ml/min.

A glass column (2 m × 4 mm I.D.) packed with 10% SP-2401 on Supelcoport (100–120 mesh) (Supelco, Bellefonte, PA, U.S.A.) was programmed with an oven temperature ramp of 65 to 100°C at 10°C/min and a final hold of 2 min. The sample injection volume was 1 μl. The attenuation was 256 at a range of 10^{-10}. The retention times, peak areas, and internal standard quantitations were determined with a Nelson Analytical Model 4400 chromatography data system (Perkin–Elmer Nelson Systems, Cupertino, CA, U.S.A.). The retention times for *n*-DBA and for the dodecane internal standard were 2.3 min and 4.4 min, respectively.

Preparation of standard solutions for GC analyses

Standards at four concentration levels ranging from 400 to 1600 μmol *n*-DBA per 25 ml toluene were prepared from stock solutions of *n*-DBA and dodecane internal standard.

Sample preparation for GC analyses

Replicate samples (at least five) of phenyl isocyanate or synthesized methyl α-isocyanatoacrylate (Fig. 1), 900–1100 μmol, were weighed accurately into 25-ml volumetric flasks. A stock solution containing 41.36 mg/ml *n*-DBA and 40.0 mg/ml dodecane, internal standard, was prepared. Five milliliters of this stock solution was pipetted into each volumetric flask. The flasks were filled to volume with toluene and the solutions mixed well. A small stirring bar was introduced into each flask, and the solutions were magnetically stirred for at least 30 min prior to injection into the GC system. Unreacted stock blanks were prepared using all reagents above except the isocyanate sample compound.

GC analysis and calculations

Samples were analyzed concurrently with multilevel standards, unreacted di-*n*-butylamine stock blanks, and internal standard blanks. Three replicate injections of each sample were made and five to nine replicate injections of each standard were made using an autosampler.

Areas for the *n*-DBA and internal standard peaks were integrated by the Nelson Analytical data system, and normal internal standard calculations and linear calibration curves were used to quantitate the amount of *n*-DBA detected. The difference in the amount of *n*-DBA detected, in μmol, between the unreacted stock blank and the reacted isocyanate sample solution also represents the molar amount of isocyanate detected.

Range and precision study

Triplicate samples of phenyl isocyanate at each of six levels were analyzed by both the GC and titration methods. The sample amounts, ranging from 25 to 1000 μmol, were obtained from serially diluted stock solutions. The data were analyzed to determine the precision of the methods at each sample amount level.

RESULTS

Comparison of GC and titration results

The percent isocyanate (NCO) contents determined for phenyl isocyanate by the GC and titration methods were:

Method	NCO (%)
GC	34.47 ± 0.31% C.V. (coefficient of variation)
Titration	34.42 ± 1.6% C.V.

The theoretical NCO content for a pure sample of phenyl isocyanate is 35.27%. The results above, expressed as sample purity are 97.73 and 97.58%, respectively. The label purity was 98+%.

The percent NCO contents determined for the synthesized methyl α-isocyanatoacrylate by the two methods are:

Method	NCO (%)
GC	30.50 ± 0.17% C.V.
Titration	30.55 ± 0.37% C.V.

The theoretical NCO content for a pure sample of methyl α-isocyanatoacrylate is 33.06%.

Statistical calculations utilizing the *t*-test at the 95% confidence level indicate no significant differences between the results obtained from the GC method and those from the titration method.

A typical GC chromatogram obtained from the reaction of phenyl isocyanate and *n*-DBA by the described method is shown in Fig. 2.

Linearity of GC method

Linear regression analysis (concentration *vs.* response defined as the peak area ratio of *n*-DBA to internal standard) was performed. The correlation coefficients for standard curves were > 0.9999.

Range and precision study

Comparison of the precision for the GC and titration methods at six different sample amounts is shown in Fig. 3. The levels of precision for the two methods at the 1000- and 500-μmol levels are quite comparable. However, below 500 μmol, the precision of the GC method was significantly better than that of the titration method. Preliminary results indicate the applicability of the GC method to a ten-fold lower

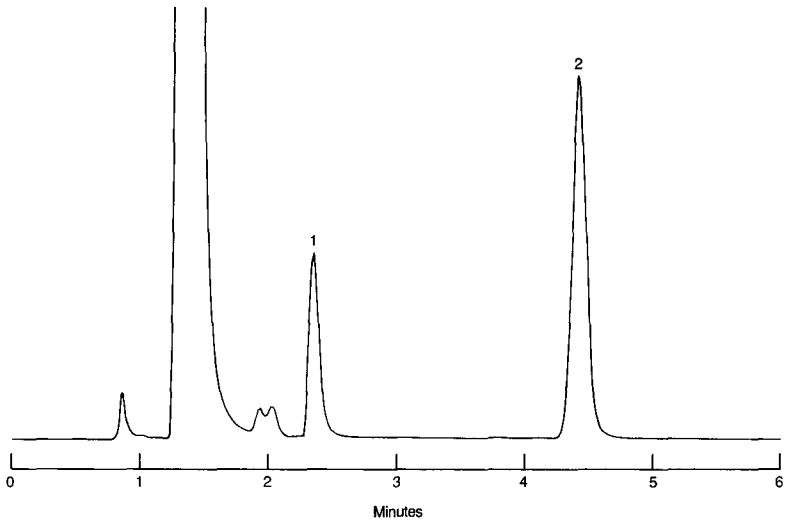


Fig. 2. Typical chromatogram obtained from the reaction of phenyl isocyanate and *n*-DBA using the reported method. Peaks: 1 = unreacted di-*n*-butylamine; 2 = dodecane, internal standard.

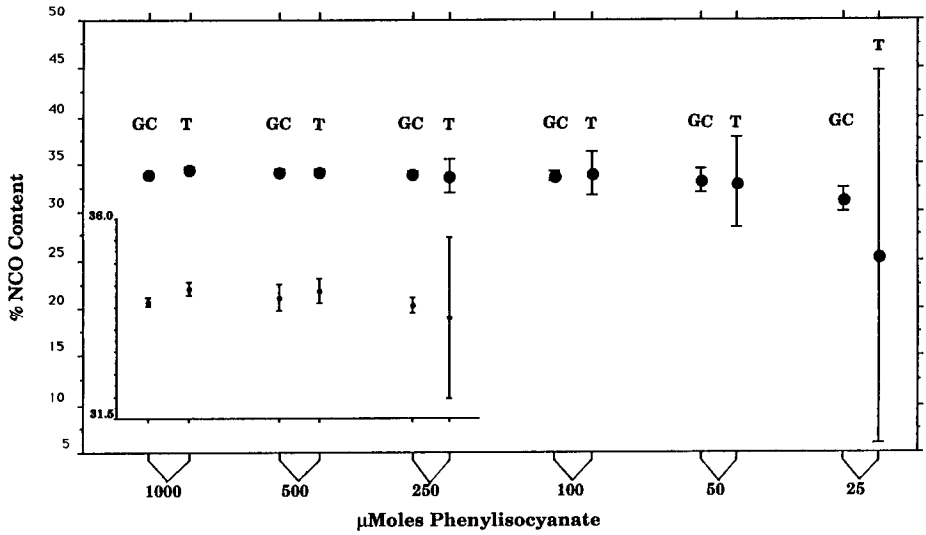


Fig. 3. Comparison of the precision of the GC and titration (T) results from triplicate samples at six sample levels. The mean results of triplicate determinations are indicated by the dots. The bracketed bars represent the confidence intervals for each set of analyses at the 95% confidence level. The inset is a scale expansion of the confidence intervals above it.

sample range. However, utilization of a GC column optimized for amine analyses may be required for the lower range application.

DISCUSSION

Method development

Several aspects of the reaction and the GC method were investigated. The completeness of the reaction was considered. Initial investigations were made to determine if a catalyst (di-*n*-butyltin dilaurate), heat (45°C), or additional reaction time would improve the *n*-DBA–isocyanate reaction. Results indicated that none of these factors had a significant effect on the extent of the reaction.

Some detection response differences were observed with different GC conditions, particularly with the injector temperature. One factor in this effect is the presence of the non-eluted urea reaction product on the column. During the GC analysis of phenyl isocyanate, the reaction product, di-*n*-butylphenyl urea (phenyl dibutyl urea), remains on the column and can cause a reduction in the amount of *n*-DBA detected in subsequent injections. The column oven temperature must be increased significantly in order to elute the urea.

No information on the boiling point of di-*n*-butylphenyl urea was found in the literature. The melting point is reported to be 85–86°C [25]. To determine the boiling point of the reaction product, a small amount was synthesized in toluene and recrystallized from ethanol. Differential scanning calorimetry (DSC) analysis of the resulting product indicated a melting point of 83.7°C (purity of 99.90 mol% [26]) and a boiling point of 267.1°C with no residue.

An injector temperature higher than the boiling point of di-*n*-butylphenyl urea was chosen (300°C) to minimize the retention of *n*-DBA during subsequent injections. Di-*n*-butylphenyl urea will elute from the column at oven temperatures of 250–270°C but does not yield a well shaped peak. Care must be taken to bake the ureas off the column periodically.

Comparison of indirect vs. direct methods

The indirect method of determining isocyanate content by reaction with *n*-DBA and subsequent quantitation of the unreacted *n*-DBA by GC has several advantages over direct GC analysis. With direct injection and detection of isocyanates, sample collection and stability are concerns because isocyanates will react readily with moisture and amines. In the indirect methods, reaction with *n*-DBA "fixes" the isocyanate concentration at that point. Direct analysis is limited to those isocyanate compounds which are volatile enough for GC and which are not thermally labile. With indirect analysis, volatility and stability are not concerns since the compound being quantitated in the GC system is the unreacted *n*-DBA, not the isocyanate.

Additionally, basing the GC method on quantitation of *n*-DBA, regardless of what isocyanate compound is being analyzed, means that the method can be applied to any isocyanate without modification of the GC parameters or column. In contrast, direct injection and detection of isocyanates or their derivatives (amines, amides, or urethanes) require that the analytical parameters be adapted to each compound of interest. With this GC analysis for *n*-DBA, however, one must determine that other compounds, such as impurities or starting materials in a synthesis reaction mixture, do not coelute with *n*-DBA or the internal standard.

A significant advantage of the indirect methods over direct methods is that no isocyanate compound is needed to generate standard solutions for calibration. This greatly reduces the amount of sample required for analysis. In fact, for the indirect methods, the isocyanate sample identity is not required.

Comparison of indirect methods —GC vs. titration

Quantitation of the GC analyses, by means of electronic integration, is inherently less subjective than quantitation of titration analyses. Also, multiple injections of each weighed sample and standard can be made with the GC method whereas only one titration can be performed per weighing. This additional data, the use of an internal standard, the ability to automate sample injection, and objective quantitation yields analytical results which are more precise.

The GC method can provide data on isocyanate content using much less sample than for a titration analysis with comparable precision.

Additionally, for isocyanate synthesis, the indirect GC method may provide more information than titrations since it may be possible to quantitate the starting materials and the *n*-DBA content concurrently, if these starting materials elute at appropriate retention times. This would provide dual confirmation of the reaction status.

CONCLUSION

The analysis method reported here appears, from data obtained on the two

sample compounds, to be a valid, precise and objective alternative to titration for the determination of isocyanate content of compounds. The method is capable of quantifying samples containing 100–1200 μmol of isocyanate. Preliminary results indicate the applicability to a 10–120-μmol range. The ability to use reduced amounts of sample, obtain higher precision, include an internal standard, and to automate the analyses are significant analytical advantages.

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