Diisocyanates 2,4-TDI and MDI

Method no.:	18
Matrix:	Air
OSHA Standard:	The current ceiling PEL for 2,4-toluene diisocyanate (2,4-TDI) and for methylene bisphenyl diisocyanate (MDI) is 0.02 ppm. This corresponds to 0.14 and 0.20 mg/m^3 for 2,4-TDI and MDI respectively. The TWA PEL is 0.005 ppm for both diisocyanates. This corresponds to 0.035 mg/m^3 for 2,4-TDI and 0.05 mg/m^3 for MDI.
Procedure:	Collection in a bubbler containing nitro reagent in toluene and analysis by high pressure liquid chromatography.
Recommended air volume and sampling rate:	20 L at 1 L/min
Detection limit of the overall procedure:	0.15 ppb (1 µg/m^3) for 2,4-TDI 0.10 ppb (1 µg/m^3) for MDI
Reliable quantitation limit:	0.3 ppb (2.4 µg/m^3) for 2,4-TDI 0.3 ppb (3.4 µg/m^3) for MDI
Standard error of estimate at the ceiling PEL:	5.5% for both 2,4-TDI and MDI
Status:	Sampling and analytical method, which has been evaluated as closely as possible to the established evaluation procedures of the Organic Methods Evaluation Branch.

Date: February 1980 Chemist: Kevin Cummins

Organic Methods Evaluation Branch
OSHA Salt Lake Technical Center
Sandy UT 84070-6406

1. General Discussion
    1.1. Background
        1.1.1. History

Analysis of aromatic diisocyanates is frequently performed by employing the Marcali or the Ranta colorimetric methods. In the past, the Marcali method has been the method of choice for the analysis of diisocyanates by the OSHA laboratory. This method employs an acidified aqueous bubbler solution to trap and convert the diisocyanates into their respective diamines. Diazotization and coupling of the diamines with N-1-naphthyl ethylenediamine produces a colored complex which is measured at two different wavelengths. The intensity of the color at the two wavelengths is a measure of the amounts of 2,4-TDI and MDI collected in the bubbler. One of the major limitations of the Marcali method is its inability to distinguish the diisocyanate from the diamine. The procedure is only applicable to aromatic isocyanates. Similarly, the Ranta method is limited by its lack of specificity. (Ref. 5.2.)

Collection and derivatization of diisocyanates in nitro reagent (0.0002 M p-nitrobenzyl-N-n-propylamine in toluene), and analysis by HPLC as developed by Dunlap, Sandridge and Keller, represented the first sensitive, specific method for the analysis of diisocyanates. (Ref. 5.3.) Highly reactive diisocyanates in the workplace air are trapped in a bubbler solution containing the nitro reagent. This secondary amine reacts readily with diisocyanates to form a stable UV absorbing urea derivative that is easily chromatographed by high pressure liquid chromatography. The method is applicable to both aromatic and aliphatic mono and diisocyanates. Analysis can be performed using either normal phase or reverse phase HPLC methods. The purpose of this evaluation is to study the sensitivity, precision, and accuracy of this method as it is routinely applied in the OSHA laboratory.

1.1.2. Toxic effects (This section is for information only and should not be taken as a basis for OSHA policy.)

Isocyanates are strong irritants and can produce an acute allergic response among some individuals. There is no data to indicate that diisocyanates are carcinogenic or teratogenic. (Ref. 5.1.) Industry sources indicate that diisocyanates yielded negative results by the Ames test for mutagenicity. (Ref. 5.4.) However, another study reported MDI to be mutagenic to **Salmonella Typhimurium** in the presence of a mammalian liver activating system, although TDI and dicyclohexylmethane 4,4'-diisocyanate showed no mutagenic activity. The NIOSH criteria document states that in the absence of supporting data, this study is insufficient evidence that diisocyanates are mutagens. (Ref. 5.1.)

1.1.3. Operations where exposure occurs

The aromatic diisocyanates TDI and MDI are widely used in the production of polyurethane foams and elastomers. Prepolymer forms of both aromatic and aliphatic diisocyanates are widely employed in the polyurethane coatings industry. (Ref. 5.5.) These prepolymer forms, while generally non-volatile, may contain varying amounts of free diisocyanates. (Ref. 5.6., 5.7.) Because of the many applications for diisocyanates, the potential for exposure is widespread.

1.1.4. Size of work population that are exposed

A 1972-74 NIOSH survey estimates that 50,000-100,000 employees in the United States were potentially exposed to diisocyanates. NIOSH indicates that this number does not include occasional users of isocyanate preparations and may underestimate the number of workers exposed. (Ref. 5.1.)

1.1.5. Physical properties (Refs. 5.8.- 5.9.)

toluene 2,4-diisocyanate	$C_9H_6N_2O_2$
molecular weight	174.15
melting point	19.5-21.5°C
flash point	152°C
solubility	dissolves in most organic solvents
structure	Figure 1.1.5.
odor	sharp, pungent, irritating

reacts with water to generate CO2

4,4'-methylenebisphenyl diisocyanate (diphenylmethane 4,4'-diisocyanate) MDI $C_{15}H_{10}N_2O_2$

molecular weight	250
melting point	37°C
specific gravity	1.97 (70°C)
structure	Figure 1.1.5.

1.2. Limit defining parameters

1.2.1. Detection limit of the analytical procedure

The detection limit of the analytical procedure is 0.3 ng per injection for both 2,4-TDI and MDI. (Section 4.1.)

1.2.2. Detection limit of the overall procedure

The detection limit of the overall procedure is 0.02 µg per sample for both 2,4-TDI and MDI. This corresponds to 0.15 ppb (1 µg/m^3) for 2,4-TDI and 0.10 ppb (1 µg/m^3) for MDI. (Section 4.2.)

1.2.3. Reliable quantitation limit

Recoveries for both 2,4-TDI and MDI are essentially 100% from bubbler solutions in the tested range of 0.04 to 10 µg of diisocyanate (2-500 µg/m^3). With optimized reverse phase HPLC analytical conditions, recoveries for a 0.048 µg spike of 2,4-TDI averaged 92.5% (SD = 6.8%) for five samples. Similarly, a 0.069 µg spike of MDI averaged 93.4% (SD = 9.9%) for six samples. These values represent the approximate lower limit for reliable quantitation under optimal analytical conditions. (Section 4.3.)

The reliable quantitation limit and detection limits reported in the method are based upon optimization of the instrument for the smallest possible amount of analyte. When the target concentration of an analyte is exceptionally higher than these limits, they may not be attainable at the routine operating parameters.

1.2.4. Sensitivity

The sensitivity of the reverse phase HPLC method over the 0.5x to 2x PEL range for 2,4-TDI and MDI is 137,849 area units for 2,4-TDI and 195,849 area units for MDI per µg/mL of analyte in acetonitrile. This is determined from the slope of the calibration curves for both 2,4-TDI and MDI standards analyzed by reverse phase HPLC. (Section 4.4.)

1.2.5. Recovery

Recovery was determined to be 100% over the 0.5x to 2x PEL range for both 2,4-TDI and MDI. This was determined from the data discussed in the next section. (Section 4.5.)

1.2.6. Precision for the analytical procedure

The pooled coefficient of variation was determined for both the reverse phase and the normal phase HPLC methods. Ten-milliliter aliquots of 0.0002 M nitro reagent in toluene placed in evaporator tubes were spiked with a mixture of 2,4-TDI and MDI. The spiked samples ranged from 1.4 µg 2,4-TDI/2.4 µg MDI to 5.8 µg 2,4-TDI/9.8 µg MDI, representing approximately 0.5x to 2x PEL for a 20-L air sample. Recovery was 100% over the entire range. The pooled coefficient of variation by the reverse phase method was 0.017 for 2,4-TDI and 0.025 for MDI over the spiked sample range. The pooled coefficient of variation by the normal phase method was 0.041 for 2,4-TDI and 0.047 for MDI over the spiked sample range. (Section 4.5.)

1.2.7. Storage

To determine the stability of the derivatized diisocyanates, 36 samples were prepared in the following manner, and analyzed over a 15-day period:

Twenty liters of air at 17°C and approximate relative humidity of 73% were pulled through 36 individual bubblers, each containing 15 mL of 0.0002 M nitro reagent in toluene. Each bubbler was then spiked with 3.02 µg 2,4-TDI and 4.31 µg MDI, representing approximately the ceiling PEL for a 20-L air sample. Six of the spiked samples were analyzed immediately by reverse phase HPLC. Half of the remaining 30 samples were stored at 2°C, the other half stored at room temperature in the dark (about 23°C). These stored samples were analyzed over a 15-day period to determine the stability of the diisocyanate derivatives with time. The results of the study indicate that 2,4-TDI and MDI are stable for at least 15 days under both refrigerated and room temperature conditions. (Section 4.6.)

1.3. Advantages

1.3.1. The sampling and analytical procedure is specific and sensitive for a wide range of isocyanates and diisocyanates employed in industry.

1.3.2. Samples are stable at room temperature, requiring no special storage requirements.

1.3.3. Reanalysis of samples is possible.

1.3.4. Multiple analysis of other isocyanates or diisocyanates is possible.

1.3.5. Analysis by two different HPLC methods for the same sample enables the analyst to gather additional confirmatory information.

1.4. Disadvantages

1.4.1. The use of toluene nitro reagent in bubblers for sampling is both cumbersome and potentially hazardous.

1.4.2. Although the collecting solution is stable for at least one month if stored in a refrigerator in a dark bottle, proper care must be taken to insure its integrity.

Prolonged exposure to light or heat may result in degradation of the nitro reagent.

2. Sampling Procedure

NOTE: Due to laboratory limitations and the potentially hazardous nature of isocyanates, a complete evaluation of the sampling procedure was not possible. The following sampling data represent a partial evaluation of the sample technique based on these limitations.

2.1. Apparatus

2.1.1. An approved and calibrated sampling pump whose flow can be determined within ±5% at the recommended flow.

2.1.2. Clean, dry 25-mL glass bubblers, fitted with ground glass joints and a fritted glass inlet.

2.1.3. Clean, dry, glass scintillation vials fitted with leak-proof Polyseal caps or other suitable glass containers for shipping samples.

2.1.4. Disposable Pasteur type glass pipettes with rubber bulb for transferring collection solution.

2.2. Reagents

2.2.1. Dry HPLC grade or UV grade toluene.

2.2.2. Coconut shell charcoal, 6-14 mesh.

2.2.3. Nitro reagent collection solution.

Nitro reagent (p-nitrobenzyl-N-n-propylamine hydrochloride) is commercially available from Regis Chemical Company. To prepare the collecting solution, dissolve 120 mg of the reagent in approximately 10 mL of HPLC grade water. Precipitate the free amine with 13 mL of 1 N NaOH. Extract the aqueous solution with HPLC grade toluene, and dry the toluene extract with anhydrous Na2SO4. Dilute the solution with toluene to 250 mL and store refrigerated in a dark bottle. The resulting solution is 0.002 M nitro reagent in toluene. Dilute 10 fold with toluene for use as collecting solution.

2.3. Sampling technique

2.3.1. Approximately 15 mL of 0.0002 M nitro reagent in toluene is placed in a clean, dry glass bubbler for sampling. The analytical procedure has enough sensitivity to permit sampling a minimum of 1 L of air. In routine sampling, however, 10 to 20 L of air is recommended. The recommended sampling rate is 1 L/min.

2.3.2. The 15 mL of toluene reagent will permit sampling for approximately 1 h at 1 L/min. If excess evaporation does occur during sampling, sampling must be interrupted and dry HPLC grade toluene added to the bubbler before resuming. Under normal conditions, it should not be necessary to add more toluene nitro reagent to the bubbler. The reagent is in sufficient excess such that an original 15 mL volume of the 0.0002 M nitro reagent in toluene contains sufficient reactive

amine to permit sampling for 8 h at 1 L/min of a work atmosphere that is 15 times in excess of the 0.005 ppm TWA PEL for either 2,4-TDI or MDI.

2.3.3. It is recommended that a glass bubbler filled with approximately 16 grams of coconut shell charcoal be placed after the sampling bubbler to trap toluene vapors. This system effectively traps toluene vapors for 1 h at a flow rate of 1 L/min at 25°C. The sampling pump must be calibrated with both the charcoal trap and the toluene nitro reagent bubbler connected in series to insure an accurate flow rate.

2.3.4. The use of tubing or cassettes in front of the inlet to the bubbler must be avoided, since diisocyanates are readily trapped by these materials (Ref. 5.10.).

2.3.5. After sampling, the collecting solution is transferred to a glass vial for shipping. Rinse the inlet tube and bubbler assembly with several 1-mL portions of toluene using a disposable Pasteur pipet. Transfer these rinses to the shipping vial.

2.3.6. Insure that the container is leak proof, and seal with the properly labeled OSHA seal.

2.3.7. Bulk samples submitted for analysis must be shipped in sealed vials and in a separate container.

2.4. Breakthrough

2.4.1. Experimental design

Due to present laboratory limitations, test atmospheres of diisocyanates cannot effectively be generated for the determination of reliable collection efficiencies. However, the following preliminary studies were done to approximate a test atmosphere.

Glass bubblers for sampling were fitted with a short piece of silanized glass tubing containing a portion of silanized glass wool. The glass tubing was butted to the inlet of the bubbler using a short piece of plastic tubing. In this manner, the exposed surface area of the plastic tubing was minimized. The glass wool was then spiked with amounts of 2,4-TDI and MDI in toluene which represent a range of 0.5 to 2 times the PEL for both analytes assuming a 20-L air sample. Twenty liters of air, at a flow rate of 1 L/min, was then drawn through the glass wool and into a bubbler containing 15 mL of collecting solution. The effects of sampling with dry and humid air were evaluated in this manner.

Air sampling was performed on a three-sampling-port manifold equipped with a probe to monitor humidity. The inlet of the bubbler, fitted with the glass tubing containing spiked glass wool, was attached to the sampling port. The outlet of the bubbler was attached to a vacuum pump. A critical orifice between the bubbler and the pump maintained a constant 1 L/min flow rate.

Dry air samples were prepared by attaching a drying tube to the manifold inlet. Humid air samples were generated by passing air through water in a controlled

temperature water bath. The humidity was monitored in the sampling manifold via the humidity probe.

2.4.2. Breakthrough results

Recoveries of triplicate 1.51, 3.02, and 5.85 µg spikes of 2,4-TDI (0.5 to 2 times the PEL) averaged 86%, 86%, and 93%, respectively, from 20 L of dry air. Recoveries for triplicate 3.02 µg an 5.85 µg spikes of 2,4-TDI (1 to 2 times the PEL) averaged 91% and 93%, respectively, from 20 L of air at 20°C and 83% relative humidity.

Recoveries for MDI spikes in the 0.5 to 2 times the PEL range were zero for both dry and humid air. This is not unexpected since MDI is a solid at room temperature, and is not volatile under these conditions.

2.4.3. Breakthrough discussion

These results indicate that nitro collecting solution effectively captures volatile 2,4-TDI. Although recoveries are not 100%, losses may be due to experimental design. It is doubtful that there is any significant breakthrough, since recovery does not decrease with an increase in 2,4-TDI concentration. No attempt was made to trap the spiked samples with a backup bubbler solution.

Surprisingly, no significant loss due to humid air was observed in this study. This may be due to a rapid volatilization and absorption in the collecting solution. In effect, the 2,4-TDI may not be significantly exposed to water to permit hydrolysis.

The data gathered in this report indicate that hydrolysis of the diisocyanates, 2,4-TDI and MDI, is not a serious problem. The storage samples prepared in Section 1.2.7. showed no decomposition either immediately, or after 15 days storage. These samples were prepared by spiking bubbler solutions that previously had 20 L of moist air drawn through them. This experiment represented the "worst possible case" for loss due to hydrolysis since the diisocyanate is introduced after moist air has been sampled. These results are consistent with the fact that secondary amines (nitro reagent) react faster than water with isocyanates (Ref. 5.11.).

2.5. Recommended air volume and sampling rate

2.5.1. The recommended air volume is 20 L.

2.5.2. The recommended sampling rate is 1 L/min.

2.6. Interferences

2.6.1. Compounds that can react with an isocyanate represent a potential interference. These would include molecules containing the following functional groups: amines, alcohols, phenols, carboxylic acids, and sulfhydryls.

2.6.2. Strong oxidizing agents can potentially destroy the nitro reagent collecting solution.

2.7. Safety precautions

Care must be exercised in sampling with bubblers containing toluene since it is a highly flammable solvent. Sampling around open flames or while smoking must be avoided.

3. Analytical Procedure

3.1. Apparatus

3.1.1. High pressure liquid chromatograph equipped with UV detector, manual or automatic sample injector, and chart recorder.

3.1.2. HPLC stainless steel columns capable of separating diisocyanate derivatives. Columns employed in this study were a 30-cm x 3.9-mm i.d. stainless steel column slurry packed with 10 µm C18 nucleosil (Macherey-Nagel, Duren, W. Germany) and a Waters 30-cm x 3.9-mm i.d. µBondapak CN column.

3.1.3. An electronic integrator, or some other suitable method of determining peak areas.

3.1.4. Small volume (1-4 mL) vials for storage and analysis of samples.

3.1.5. Microliter syringes (10-100 µL) for sample injection.

3.1.6. Temperature controlled water bath equipped with nitrogen stream drying needles.

3.1.7. Evaporator tubes, 10 mL or larger.

3.1.8. Rotary evaporator for stripping off organic solvents.

3.1.9. Volumetric pipettes and flasks for preparation of standards.

3.1.10. Suitable glassware for preparation of nitro reagent and for preparation of diisocyanate urea derivatives.

3.2. Reagents

3.2.1. Reagent grade phosphoric acid.

3.2.2. 1 N NaOH.

3.2.3. HPLC grade methanol, n-heptane, toluene, methylene chloride, isopropanol, hexane, acetonitrile, and isooctane.

3.2.4. HPLC grade water. Our laboratory employs a commercially available water filtration system for the preparation of HPLC grade water.

3.2.5. 2,4-TDI, Lot #176445-A, K&K Labs, Plain View, N.Y.

3.2.6. Recrystallized MDI.

3.2.7. p-Nitrobenzyl-N-n-propylamine hydrochloride from Regis Chemicals, Morton Grove, IL.

3.3. Standard preparation

3.3.1. Recrystallization of MDI.

MDI for derivative formation is recrystallized according to the procedure of Vogt (Ref. 5.12.): 5 g of MDI is dissolved in 30 mL of methylene chloride and filtered. The undissolved residue is discarded. The methylene chloride solution is

concentrated to 5 to 10 mL. A small amount of n-heptane is added to start precipitation. The MDI precipitate is filtered and dried under vacuum.

3.3.2. The diisocyanate urea derivatives for use as standards are prepared according to the method of Vogt (Ref. 5.12.)

2,4-TDI urea derivative preparation:

One gram of p-nitrobenzyl-N-n-propylamine hydrochloride is extracted into 50 mL of toluene as described in Section 2.2.3. for the preparation of collecting solution. A solution of 0.31 g/30 mL of 2,4-TDI in toluene is slowly mixed with the nitro reagent (2.5 molar excess). The precipitate formed is filtered and redissolved in a minimal volume of methylene chloride. Hexane is added to the solution to initiate precipitation. The precipitate is filtered and washed with hexane (approximate yield is 150 mg of 2,4-TDI urea derivative).

MDI urea derivative preparation:

Two and four-tenths grams of p-nitrobenzyl-N-n-propylamine hydrochloride is extracted into 50 mL of n-heptane in a manner analogous to the preparation of nitro collecting solution (Section 2.2.3.). One and three-tenths grams recrystallized MDI/25 mL methylene chloride solution is slowly added to the heptane nitro reagent solution with stirring (molar excess 2.1 to 1). The precipitated MDI urea derivative is filtered and washed with methylene chloride. This derivative can be recrystallized by redissolving in methylene chloride and reprecipitating with n-heptane. Yield is approximately 1 g.

3.3.3. Preparation of working range standards

A stock standard solution is prepared by dissolving 2,4-TDI and MDI urea derivatives in acetonitrile for reverse phase HPLC analysis, and in methylene chloride for normal phase HPLC analysis. To express the derivative as free diisocyanate, the amount of 2,4-TDI urea weighed is multiplied by the correction factor 0.310.

$$\frac{\text{MW 2,4-TDI}}{\text{MW 2,4-TDI urea}} = \frac{174}{562} = 0.310$$

Similarly, the correction factor for MDI urea is 0.392

$$\frac{\text{MW MDI}}{\text{MW MDI urea}} = \frac{250}{638} = 0.392$$

If the urea derivatives of the diisocyanates are not available, working range standards of the derivatives can be prepared from nitro reagent and the free diisocyanate standard. The following is a suggested method for their preparation:

Prepare a stock solution of the diisocyanate in the 0.1 to 0.5 mg/mL range by dissolving the diisocyanate in dry methylene chloride. Aliquots of this stock solution are then reacted with a twofold molar excess of nitro reagent in methylene chloride. (Nitro reagent in methylene chloride is prepared in the same manner as nitro collecting solution, Section 2.2.3. by substituting methylene chloride for toluene.)

For normal phase analysis, the derivatized diisocyanate in methylene chloride can be used as a standard. For reverse phase analysis, the methylene chloride is evaporated, and the diisocyanate urea derivative formed is redissolved in acetonitrile.

3.4. Sample preparation

3.4.1. The entire volume of the toluene nitro collecting solution is transferred to a 50-mL 24/40 taper round bottom flask using several small volumes of toluene to achieve the transfer. The flask is attached to a rotary evaporator and the contents are taken to dryness.

3.4.2. The dried sample is redissolved in several milliliters of methylene chloride and the solution is transferred to a 10-mL evaporator tube. Several additional small volumes of methylene chloride are used to thoroughly rinse the flask. The sample in the evaporator tube is taken to dryness in a 45°C water bath equipped with N2 stream drying needles.

3.4.3. For normal phase HPLC analysis, exactly 1 mL of methylene chloride is pipetted into the tube and the sample is thoroughly vortexed. The solution is then transferred to a small capped vial for analysis. For reverse phase analysis, 1 mL of acetonitrile is used in place of methylene chloride.

3.5. Analysis

Note: The recommended analytical method for isocyanates is the reverse phase method. The normal phase method is included as an alternate method.

3.5.1. Reverse Phase HPLC Conditions (Figure 4.7.1.)

column:	30-cm x 3.9-mm stainless steel column, slurry packed with 10L C18 Nucleosil (Macherey-Nagel; Duren, W. Germany) or suitable replacement.
mobile phase:	73/26.9/0.1 methanol/water/phosphoric acid (v/v/v)
flow rate:	1 mL/min
UV detector:	254 nm
injection size:	10-30 µL

3.5.2. Normal phase HPLC conditions (Figure 4.7.2.)

column:	Waters µBondapak CN, 30 cm x 3.9 mm or a suitable replacement.
mobile phase:	isooctane/isopropanol/methanol 75/10/15 (v/v/v)
flow rate:	1 mL/min
UV detector:	254 nm
injection size:	25 µL

3.5.3. Analysis discussion

In the past, the normal phase method developed in our laboratory was employed. The reverse phase method now recommended is an adaptation of a method developed by Sango. (Ref. 5.13.) The use of acid in the mobile phase serves to protonate the secondary amine of the excess nitro reagent and causes it to elute with the solvent front. For some types of reverse phase packing materials, it is necessary to make the methanol/water mobile phase 1% in triethylamine and adjust the pH to 3 with phosphoric acid as described by Sango. The binding of the nitro reagent to the column may be caused by an interaction of the amine with exposed silica sites. With some packing materials, a simple pH adjustment serves to elute the nitro reagent, whereas in other cases it is necessary to effectively coat all the active binding sites using a non-UV absorbing protonated tertiary amine in the mobile phase. Spherisorb 10-µm ODS, and Waters Radial Pak A (reverse phase), both require triethylamine in the mobile phase, while Waters µBondapak C18 and Nucleosil C18 do not.

It should also be recognized that in the normal phase method, the nitro reagent does not elute early. Late elution can interfere with the routine sample analysis and also cause baseline drift problems.

Finally, Figure 4.7.3. demonstrates the separation of 2,4- and 2,6-TDI isomers by reverse phase. We have not achieved this separation using the CN column, however, it is easily accomplished using reverse phase techniques. Since industrial applications employ an isomeric mixture of 2,4- and 2,6-TDI, the ability to achieve the separation is important.

3.6. Interferences

3.6.1. Any compound having the same retention time as the standards is a possible interference. Generally, chromatographic conditions can be altered to separate an interference. The reverse phase method is especially flexible in this regard

since it is more selective for isocyanate-urea derivatives than the normal phase method.

3.6.2. Retention time data on a single column is not proof of chemical identity. Analysis by alternate column system, ratioing of wavelength response using a dual channel UV detector, and ultimately mass spectrometry are additional means of identity. (See UV spectra for 2,4-TDI and MDI derivatives, Figure 4.8.)

3.7. Calculations

The concentration in µg/mL of 2,4-TDI and MDI present in a sample is determined from the area response of the analytes as measured by an electronic integrator. Comparison of sample response with a least squares curve fit for standards allows the analyst to determine the concentration of diisocyanate in µg/mL for the sample. Since the sample volume is 1 mL, the results in µg/m^3 of air are expressed:

$$\frac{(\mu g/mL \text{ diisocyanate})\ (1\ mL)}{\text{air volume, L}} \times \frac{1000\ L}{1\ m^3} = \frac{\mu g}{m^3}$$

3.8. Safety precautions

3.8.1. Sample and standard preparations should be done in a hood. Avoid exposure to the diisocyanate standards.

3.8.2. Avoid skin contact with all solvents.

3.8.3. Wear safety glasses at all times.

4. Backup Data

4.1. Detection limit of the analytical procedure

The detection limit for the analytical procedure was determined by injecting 30 µL of 0.012 µg/mL 2,4-TDI, 0.016 µg/mL MDI standard mixture prepared in acetonitrile. The detection limit is 0.3 ng per injection for both 2,4-TDI and MDI. This response is approximately five times the baseline noise level determined by peak height measurement. (Figure 4.1.)

4.2. Detection limit of the overall procedure

The detection limit of the overall procedure is determined to be the amount of analyte spiked in a bubbler which can be detected at the analytical detection limit.

Table 4.2.
Detection Limit Data

2,4-TDI (µg)		MDI (µg)	
amount spiked	amount recovered	amount spiked	amount recovered
0.017	0.016	0.028	0.029
0.048	0.042	0.069	0.056
0.048	0.042	0.069	0.074
0.096	0.096	0.14	0.12
0.096	0.075	0.14	0.12
0.190	0.185	0.28	0.28
0.190	0.189	0.28	0.27

Linear plots of the data in Table 4.2. result in an overall detection limit of 0.02 µg per sample for both 2,4-TDI and MDI.

4.3. Reliable quantitation limit

The data presented below shows the % recovery and precision for samplers spiked with 0.048 µg of 2,4-TDI, the reliable quantitation.

Table 4.3.1.
RQL Data for 2,4-TDI

% recovery		
87.5		
87.5	X	= 92.5
100.0	SD	= 6.8
100.0	1,96(SD)	= 13.3
87.5		

The data presented below shows the % recovery and precision for samplers spiked with 0.069 µg of MDI, the reliable quantitation limit.

Table 4.3.2.
RQL Data for MDI

% recovery			
81.2			
107.0	X	=	93.4
98.6	SD	=	9.9
95.6	1,96(SD)	=	19.4
95.6			
82.6			

4.4. Sensitivity

Table 4.4.1.
2,4-TDI Standards in Acetonitrile and Their Area Response

0.549 µg/mL	1.10 µg/mL	2.20 µg/mL	5.49 µg/mL	10.98 µg/mL
70,967	149,529	314,329	761,687	1,516,850
76,069	168,730	319,263	773,831	1,514,600
	157,975	313,749	773,433	
	155,228	311,942		

Table 4.4.2.
MDI Standards in Acetonitrile and Their Area Response

0.588 µg/mL	1.18 µg/mL	2.35 µg/mL	5.88 µg/mL	11.77 µg/mL
109,858	230,223	472,616	1,160,002	2,306,632
	235,266	459,047	1,135,657	2,307,841
	235,240	463,450	1,142,479	
	235,413	467,982		

The calibration curves for 2,4-TDI and MDI in the 0.5 to 2x PEL range using the above data are shown in Figures 4.4.1. and 4.4.2., respectively. The slope of the line represents the sensitivity of the analyte by the reverse phase method.

4.5. Precision and recovery

Table 4.5.1.
Precision and Recovery Data
for 2,4-TDI Using Reverse Phase HPLC

x PEL	0.5x	1x	2x
µg/sample	1.44	2.89	5.78
µg recovered	1.41	2.90	5.73
	1.40	2.95	5.75
	1.45	2.87	5.80
	1.48	2.92	5.74
	1.45	2.90	5.81
	1.39	2.97	
X	1.43	2.92	5.80
SD	0.035	0.037	0.036
CV	0.025	0.013	0.063

CV = 0.017

Table 4.5.2.
Precision and Recovery Data
for MDI Using Reverse phase HPLC

x PEL	0.5x	1x	2x
µg/sample	2.40	4.89	9.78
µg recovered	2.36	4.78	9.40
	2.37	4.85	9.41
	2.39	4.71	9.53
	2.39	4.80	9.77
	2.34	4.83	9.47
	2.57	5.00	9.77
X	2.40	4.83	9.56
SD	0.084	0.097	0.17
CV	0.035	0.020	0.018

CV = 0.025

Table 4.5.3.
Precision and Recovery Data
for 2,4-TDI Using Normal Phase HPLC

x PEL	0.5x	1x	2x
µg/sample	1.44	2.89	5.78
µg recovered	1.52	3.02	5.52
	1.42	2.87	5.59
	1.42	2.86	5.84
	1.40	2.96	5.97
	1.50	3.12	5.99
	1.33	3.12	6.07
	1.37	2.98	6.13
	1.52	2.95	6.22
	1.52	2.99	6.24
	1.49	3.03	
	1.45	2.96	5.95
X	0.070	0.080	0.25
SD	0.048	0.027	0.043
CV			
CV = 0.041			

Table 4.5.4.
Precision and Recovery Data
for MDI Using Normal Phase HPLC

x PEL	0.5x	1x	2x
µg/sample	2.40	4.89	9.78
µg recovered	1.54	5.09	9.18
	2.55	4.79	9.31
	2.39	5.05	9.70
	2.30	4.95	9.70
	2.58	5.23	9.95
	2.20	5.00	10.02
	2.26	5.03	10.35
	2.60	5.20	10.39
	2.60	5.07	2.51
X	2.45	5.05	9.92

SD	0.15	0.13	0.44
CV	0.062	0.026	0.044

CV = 0.046

These results indicate that the average recovery for both 2,4-TDI and MDI is essentially 100% in the 0.5x PEL to 2x PEL range.

4.6. Storage Test

Tables 4.6.1. and 4.6.2. show the percent recoveries for 2,4-TDI and MDI spiked samples stored at refrigerated and ambient temperatures. (Section 1.2.7.) These results are presented graphically in Figures 4.6.1.- 4.6.4.

Table 4.6.1.
Storage Tests for 2,4-TDI (3.02 µg Spike)

storage time (days)	% recovery (refrigerated)			(ambient)		
0	98.7	98.7	98.3	101.0	104.0	105.0
3	98.7	99.3	103.0	100.0	101.0	104.0
6	103.0	105.0	103.0	100.0	103.0	101.0
10	98.0	98.3	101.0	99.7	97.3	99.6
13	101.0	99.7	98.7	101.0	99.0	97.7
17	97.0	91.3	98.0	101.0	98.0	97.3

Table 4.6.2.
Storage Tests for MDI (4.31 µg Spike)

storage time (days)	% recovery (refrigerated)			(ambient)		
0	102.0	102.0	101.0	102.0	105.0	109.0
3	97.0	95.1	101.0	99.3	99.3	99.1
6	102.0	99.1	101.0	101.0	101.0	101.0
10	99.1	97.2	101.0	99.3	96.5	100.0
13	98.6	98.8	96.8	103.0	97.9	97.9
17	95.3	93.7	99.5	101.0	100.0	99.5

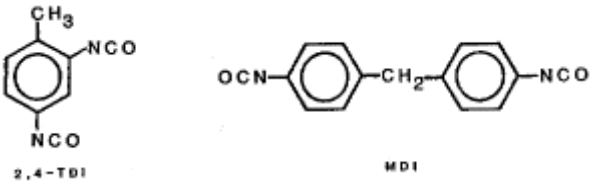

Figure 1.1.5. Molecular structures for 2,4-TDI and MDI.

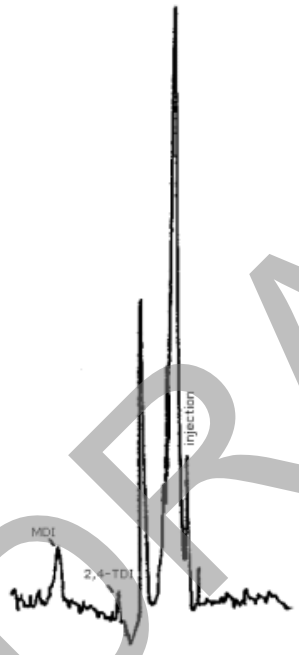

Figure 4.1. Detection limit for analytical procedure.

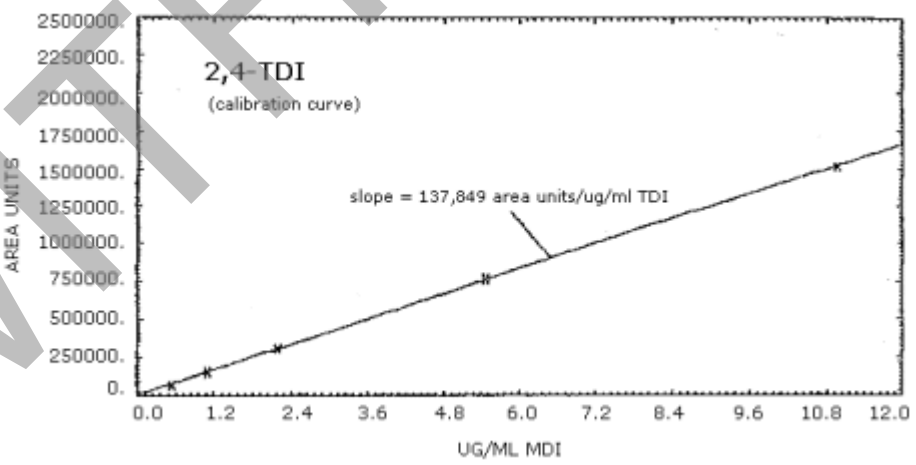

Figure 4.4.1. Calibration curve for 2,4-TDI.

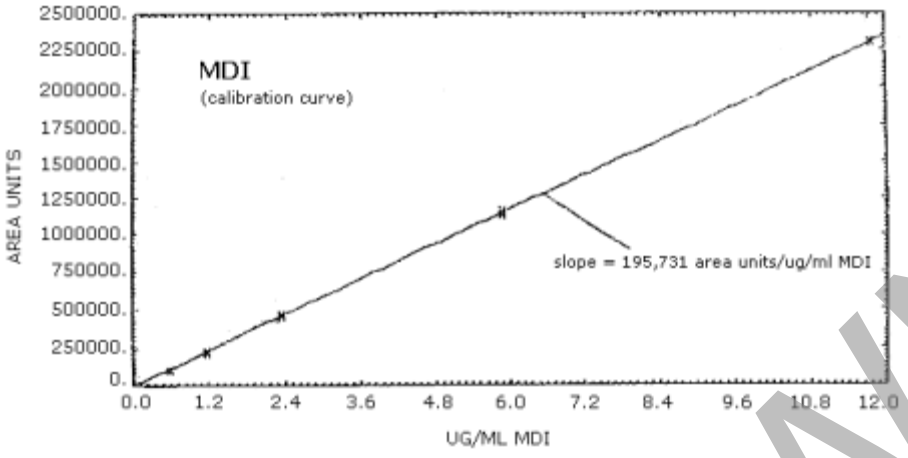

Figure 4.4.2. Calibration curve for MDI.

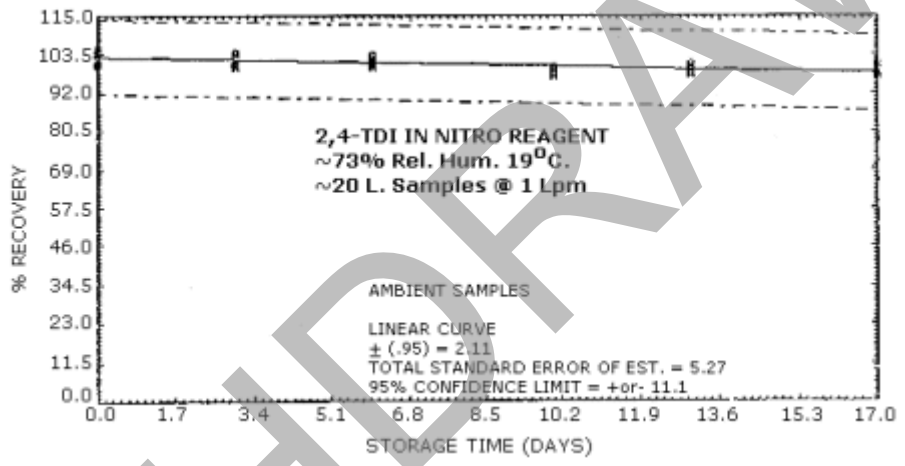

Figure 4.6.1. Ambient storage for 2,4-TDI.

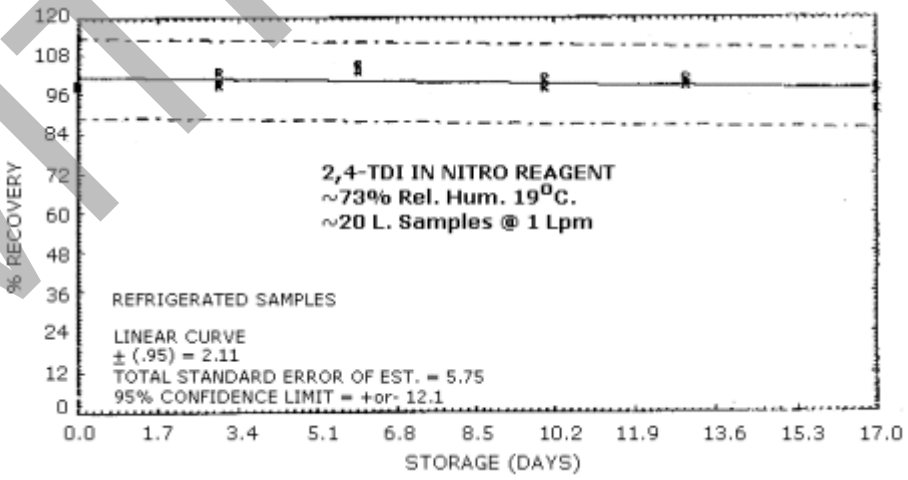

Figure 4.6.2. Refrigerated storage for 2,4-TDI.

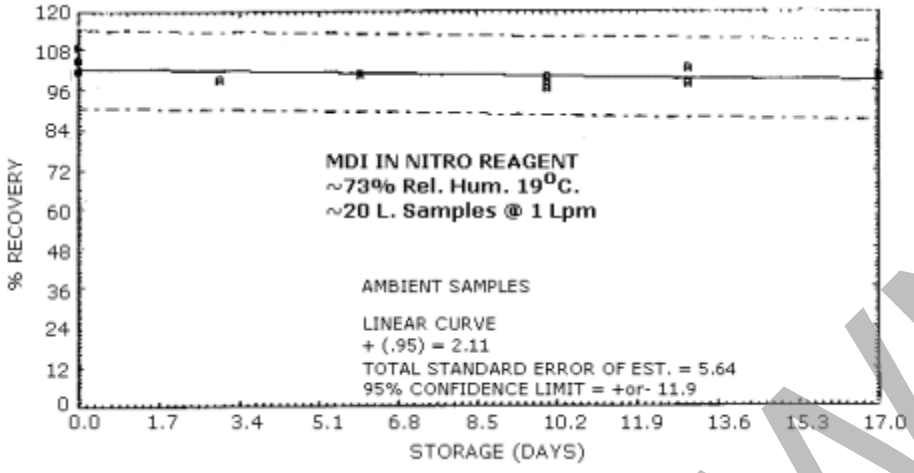

Figure 4.6.3. Ambient storage for MDI.

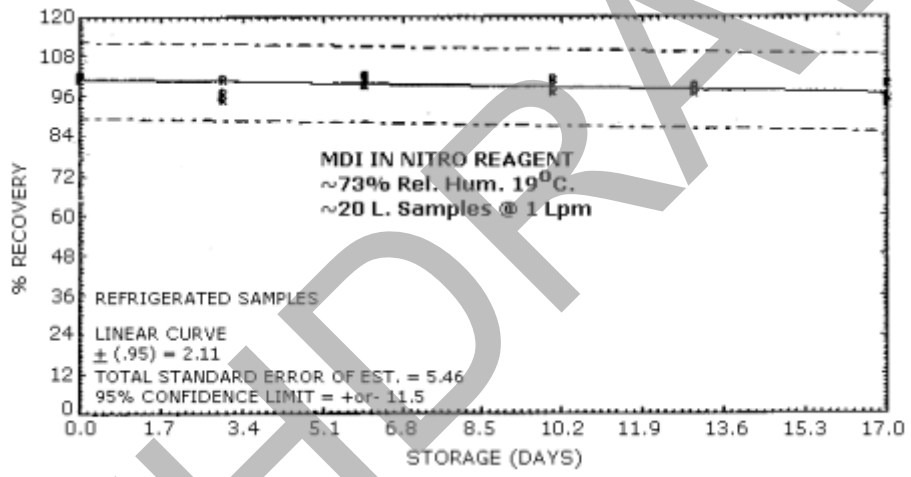

Figure 4.6.4. Refrigerated storage for MDI.

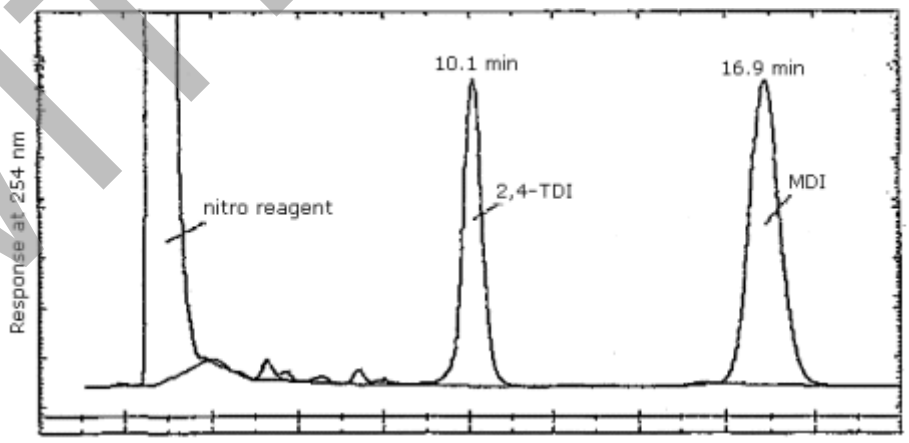

Figure 4.7.1. Reverse phase separation of 2,4-TDI and MDI derivatives.

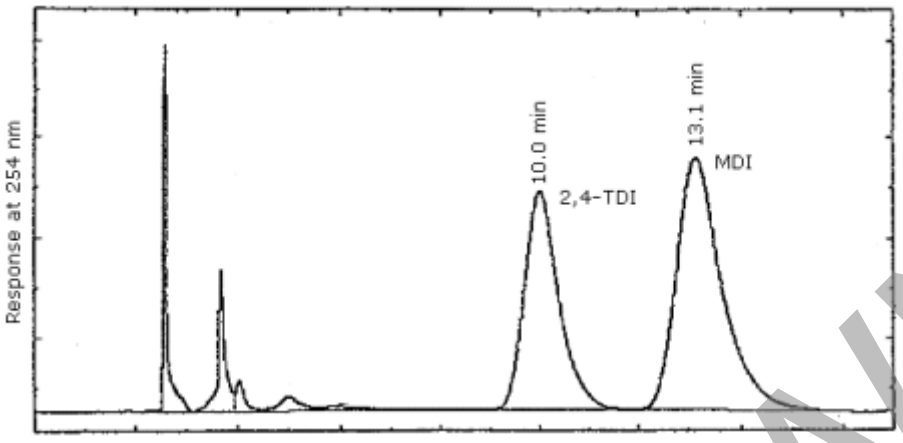

Figure 4.7.2. Normal phase separation of 2,4-TDI and MDI derivatives.

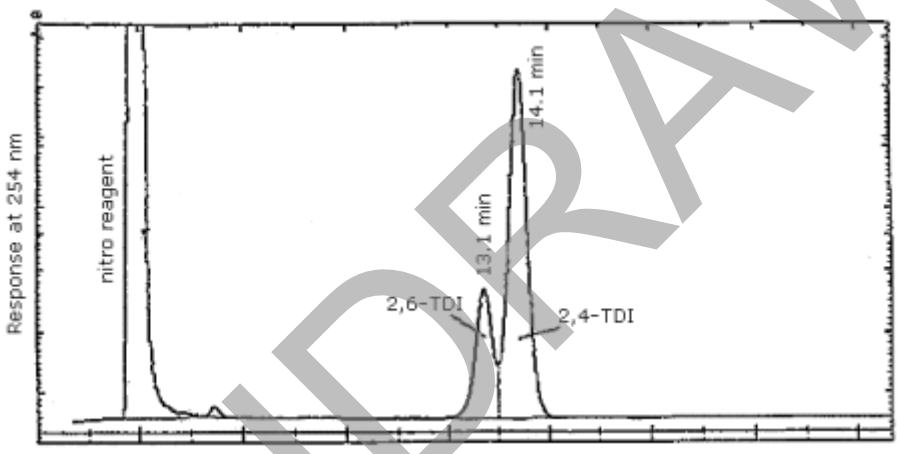

Figure 4.7.3. Reverse phase separation of 2,4- and 2,6-TDI derivatives. Same conditions as in Section 3.5.1. except the mobile phase is methanol/water/phosphoric acid 70/29.9/0.1 (v/v/v).

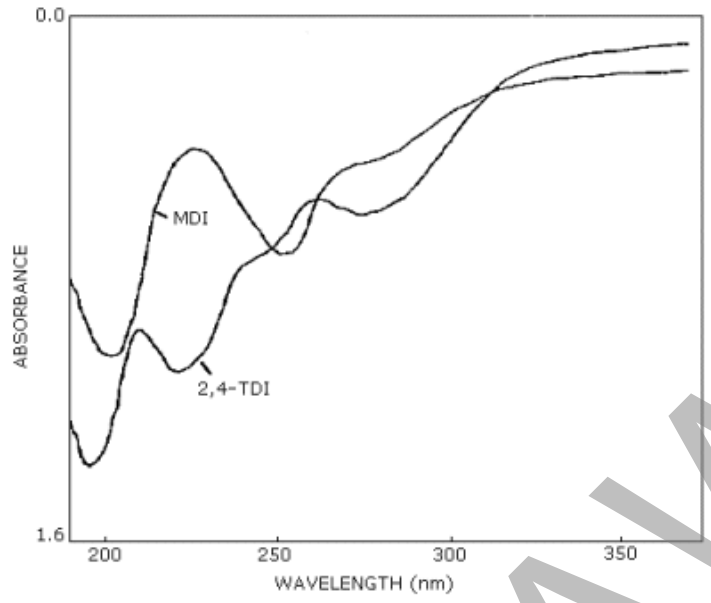

Figure 4.8. UV spectra of 2,4-TDI and MDI derivatives in acetonitrile.

5. References

5.1. NIOSH Criteria Document On Diisocyanates, DHEW, (NIOSH) Publication No. 78-215, DHEW, Public Health Service, Center for Disease Control, NIOSH, September, 1978.

5.2. NIOSH Criteria Document On Toluene Diisocyanate, HSM 73-11022, DHEW, Public Health Service, Center for Disease Control, NIOSH, 1973.

5.3. Dunlap, Sandridge and Keller, **Anal. Chem.**, 48, 497, 1976.

5.4. "The Pros and Cons of Urethane Coatings", Mobay Chemical Corporation, Plastics and Coatings Division, Pittsburgh, PA 15205.

5.5. "Chemistry for Coatings", Mobay Chemical Corporation, Plastics and Coatings Division, Pittsburgh, PA 15205.

5.6. McFadyen, P., **J. Chromatogr.**, 123, 468, 1976.

5.7. Spangnolo, Frank, **J. Chromatogr. Sci.**, 14, 52, 1976.

5.8. The Merck Index, 9th Edition, Merck and Company, Rahway, NJ, 1976.

5.9. The Condensed Chemical Dictionary, 9th Edition, Hawley, Gessner, Van Nostrand Reinhold Co., N.Y., NY, 1977.

5.10. Telephone Conversation with Bob Sandridge, Mobay Chemical, New Martinsville, WV 28155, September, 1979."

5.11. Urethane Polymers", V. 21, p. 64, Kirk-Othmer Encyclopedia of Chemical Technology, 2nd Edition, Interscience Publishers, 1970.

5.12. Vogt, C.R. Hastings, "Modification of an Analytical Procedure for Isocyanates to High Speed Liquid Chromatography", NIOSH Contract CDC-210-75-0052, University of Missouri, Columbia, MO, April, 1978.

5.13. Sango, **J. Liq. Chromatogr.**, 2(6), 763, (1979).