Journal of Chromatography, 190 (1980) 175–182

CHROM. 12,502

Note

Determination of airborne free monomeric aromatic and aliphatic isocyanates by high-performance liquid chromatography

D. A. BAGON and C. J. PURNELL

Health and Safety Executive, Occupational Medicine and Hygiene Laboratories, 403–405 Edgware Road, London NW2 6LN (Great Britain)

(First received June 11th, 1979; revised manuscript received October 22nd, 1979)

Isocyanates are used in the production of flexible and rigid foams, polyurethane paints and adhesives. They are known to irritate the respiratory tract and can produce asthma-like symptoms in sensitised workers even at low concentrations in air. Various methods have been published for measuring isocyanates in air at these levels[1–5].

This paper describes two high-performance liquid chromatography (HPLC) methods that are currently employed routinely in the authors' laboratory for the measurement of free monomeric isocyanates in air. The first method utilises the well-known nitro reagent[3] and is based on the reaction of both aromatic and aliphatic isocyanates with N-(4-nitrobenzyl)-N-*n*-propylamine (nitro reagent) to form stable urea derivatives. Acetylation of the excess nitro reagent overcomes the problem of column deterioration and tailing of the nitro reagent on the column. This enables isocratic elution to be used in preference to gradient elution previously recommended[5]. The second method uses ethanol as the reagent. Aromatic isocyanates react with the ethanol to form strongly UV-absorbing ethyl urethane derivatives. This fact was first utilised by Goldberg and Maddison[4] in developing an HPLC method for these isocyanates in air. We have modified their method to increase the sensitivity for these isocyanates.

EXPERIMENTAL

Chromatographic apparatus

The liquid chromatograph consisted of a Waters 6000A constant-flow, reciprocating diaphragm pump, a stopped-flow injection system, and a Cecil Instruments CE2012 ultraviolet detector. LiChrosorb Si 60 (5 μm average size, BDH, Poole, Great Britain) was packed into a stainless-steel column (150 × 4.5 mm I.D.) by a high-pressure slurry technique[7]. The mobile phase was deaerated and pumped at ambient temperature through the column at a flow-rate of 1.5 ml/min.

Mobile phase

Two mobile phases were used. Mobile phase A consisted of 10% ethanol in 2,2,4-trimethylpentane and was used for the separation of the nitro reagent urea derivatives. Mobile phase B consisted of 0.5% methanol in dichloromethane and was used for the separation of the ethyl urethane derivatives.

Isocyanates

The following isocyanates were used: Hexamethylene diisocyanate (HDI), Desmodur H, Bayer, Richmond upon Thames, Great Britain; toluene diisocyanate (TDI), Fluka, Buchs, Switserland; phenyl isocyanate (PI), Eastham-Kodak, Rochester, N.Y., U.S.A.; isophorone diisocyanate (IPDI), Veba-Chemie, Gelsenkirchenvuer, G.F.R. and 4,4'-diisocyanate-diphenylmethene (MDI), I.C.I., Macclesfield, Great Britain.

Reagents for derivatisation

N-(4-Nitrobenzyl)-N-n-propylamine (nitro reagent) absorber solution[5] (A). A 120-mg amount of N-(4-nitrobenzyl)-N-*n*-propylamine hydrochloride (Phase Separations, Queensferry, Great Britain) was dissolved in 10 ml of distilled water. Then 13 ml of aqueous 1 *M* sodium hydroxide was added to precipitate the free amine which was then extracted with 4 × 50 ml of toluene. These extracts were combined, made up to 250 ml with toluene and dried over sodium sulphate overnight. This solution was then diluted 10-fold with dry toluene to give the $2 \cdot 10^{-4}$ *M* absorber solution. This was stored in the dark and a fresh solution prepared every ten days.

Ethanol absorber solution (B). Ethanol (Burrough, London, Great Britain) was used without further purification.

Preparation of standard solutions

Urea derivative solutions (A). A 0.1-g amount of the appropriate isocyanate of known purity was accurately weighed and made up to 25 ml with dry toluene. Subsequent dilutions were made so that 0.5 ml of each dilute solution when added to 10 ml of the nitro reagent absorber solution yielded standard urea solutions in the range 1.6–4.0 μg/ml. The mixtures were shaken and left overnight to complete the reaction. One drop of acetic anhydride was added to each of the standards to convert the unreacted nitro reagent to its acetyl derivative. 2 ml of each urea solution were measured into 2-ml micro-reaction vessels, evaporated to dryness with nitrogen and the ureas redissolved in 0.2 ml of dry dichloromethane.

Ethyl urethane derivative solutions (B). Ethyl urethane derivatives of the aromatic isocyanates were prepared by the method described by Bagon and Hardy[6]. 0.01 g of each ethyl urethane prepared was weighed and dissolved in 25 ml of ethanol. Each solution was then diluted in the appropriate volume of dichloromethane to yield standard ethyl urethane concentrations in the range 2–5 μg/ml.

Air sampling and sampling preparation

A 10-ml volume of the appropriate absorber solution (A or B above) was placed in a midget impinger (Greenburg-Smith) or sintered-bubbler. Air containing isocyanate was sampled at 1 l/min to give a 10 l or more air sample. After sampling, 2 ml of the absorber solution were measured into a 2-ml micro-reaction vessel and evaporated to dryness with nitrogen (in the case of the nitro reagent absorber solution (A), one drop of acetic anhydride was added prior to evaporation). The residue was then redissolved in 0.2 ml of dry dichloromethane.

Determination of collection efficiency

Atmospheres of isocyanate were generated by the syringe injection or diffusion cell methods[5]. These atmospheres were drawn at 1 l/min through two midget im-

pingers in series, each containing 10 ml of the appropriate reagent (A or B) under test. After sampling at least 10 l of air through the impingers, each absorber solution was analysed for the appropriate isocyanate derivative and the extent of breakthrough determined.

RESULTS AND DISCUSSION

Nitro reagent method for aliphatic and aromatic isocyanates in air (A)

In a previous study, Hastings-Vogt *et al.*[5] reported that the unreacted nitro reagent progressively reduced column performance and tailed badly on the column. This was not overcome by gradient elution and necessitated extended analysis time for complete elution of the reagent. In order to overcome this problem they recommended the use of *p*-tolyl isocyanate as a scrubber to react with the unreacted nitro reagent. The resulting urea derivative had a much shorter retention time. The addition of an isocyanate however is not ideal and could be an added complication in work with atmospheres containing mixed isocyanates, so an alternative scrubber was sought. Acetic anhydride was found to be most useful. It reacts fully with the nitro reagent

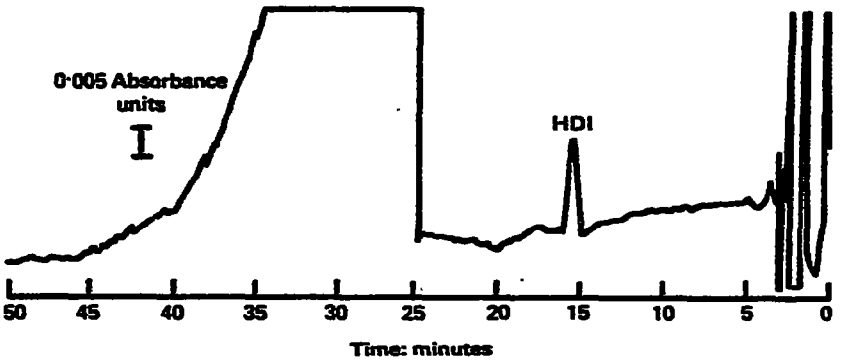

Fig. 1. Chromatogram of a HDI–urea sample; no acetic anhydride added. Conditions: column, 150 × 4.5 mm I.D., LiChrosorb Si 60; mobile phase, ethanol–2,2,4-trimethylpentane (9:91); temperature, ambient; flow-rate, 1.5 ml/min; amount injected, 20 µl; detection, 270 nm.

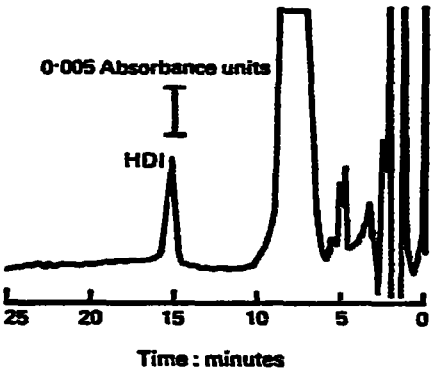

Fig. 2. Chromatogram of a HDI–urea sample; acetic anhydride added. Conditions as in Fig. 1.

to form N-4-nitrobenzyl propanilide which elutes quickly from the column enabling an isocratic solvent system[10] to be used.

Fig. 1 shows a chromatogram of an HDI–urea sample with unreacted nitro reagent present, Fig. 2 shows the same HDI–urea sample but with acetic anhydride added. The acetic anhydride has no effect on the amount of HDI–urea present, the peak height being the same in both cases. The same column was used throughout the study, no deterioration in performance was noted.

The nitro reagent method may be used to sample both aromatic and aliphatic isocyanates in air. Fig. 3 shows a chromatogram of a mixture of isocyanates–ureas with baseline separation from the nitro reagent acetyl derivative (NRAD). Table I lists the retention times and detection limits for these isocyanate–urea derivatives.

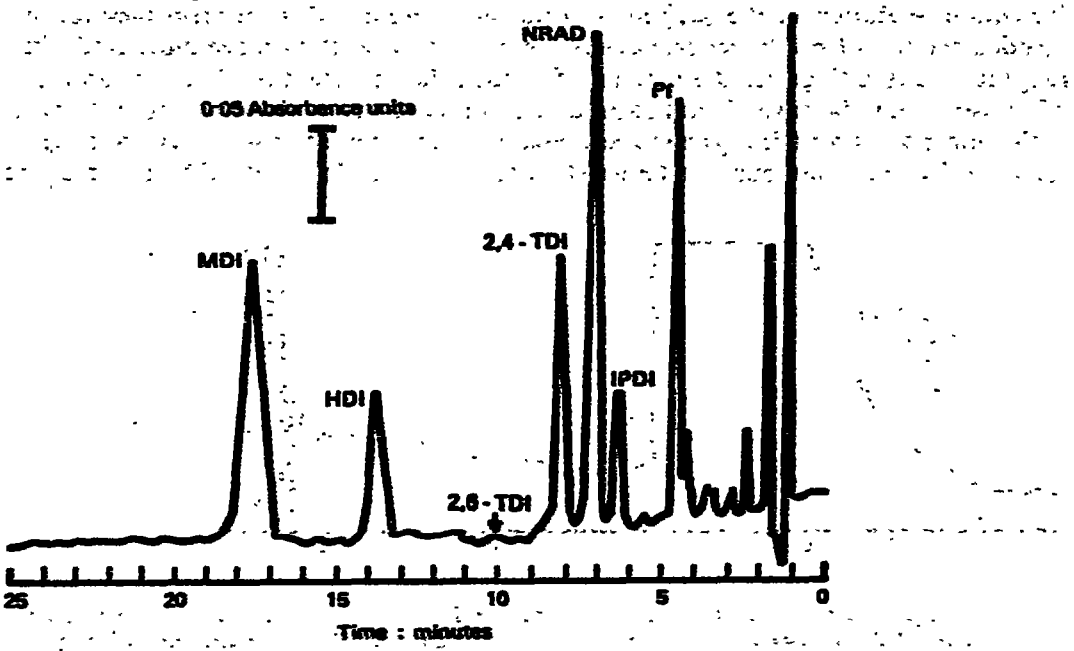

Fig. 3. Chromatogram of aromatic and aliphatic isocyanate–ureas. Conditions as in Fig. 1, except: mobile phase, ethanol–2,2,4-trimethylpentane (10:90); detection, 254 nm.

TABLE I

RETENTION TIME DATA AND DETECTION LIMITS FOR ISOCYANATE–UREA DERIVATIVES

For conditions, see Fig. 3.

Compound	*Retention time (min)*	$\lambda_{max.}$	*Detection limit for 10-l air sample (μg/m³)*
PI–urea	4.4	244	5
IPDI–urea	6.3	272	10
Nitro reagent Acetyl derivative	7.1	268	—
TDI–urea	8.1	248	10
HDI–urea	13.6	270	5
MDI–urea	17.4	254	10

Although the method may be applied to both aromatic and aliphatic isocyanates our use of the method has been primarily for the measurement of aliphatic isocyanates, particularly HDI. This particular isocyanate is one of the least reactive with the nitro reagent[5]. The collection efficiency for HDI with our impinger–nitro reagent absorber system was determined and was found to be 95%. This agrees with previous workers[5].

Our routine use of the nitro reagent method has covered a wide range of pro-

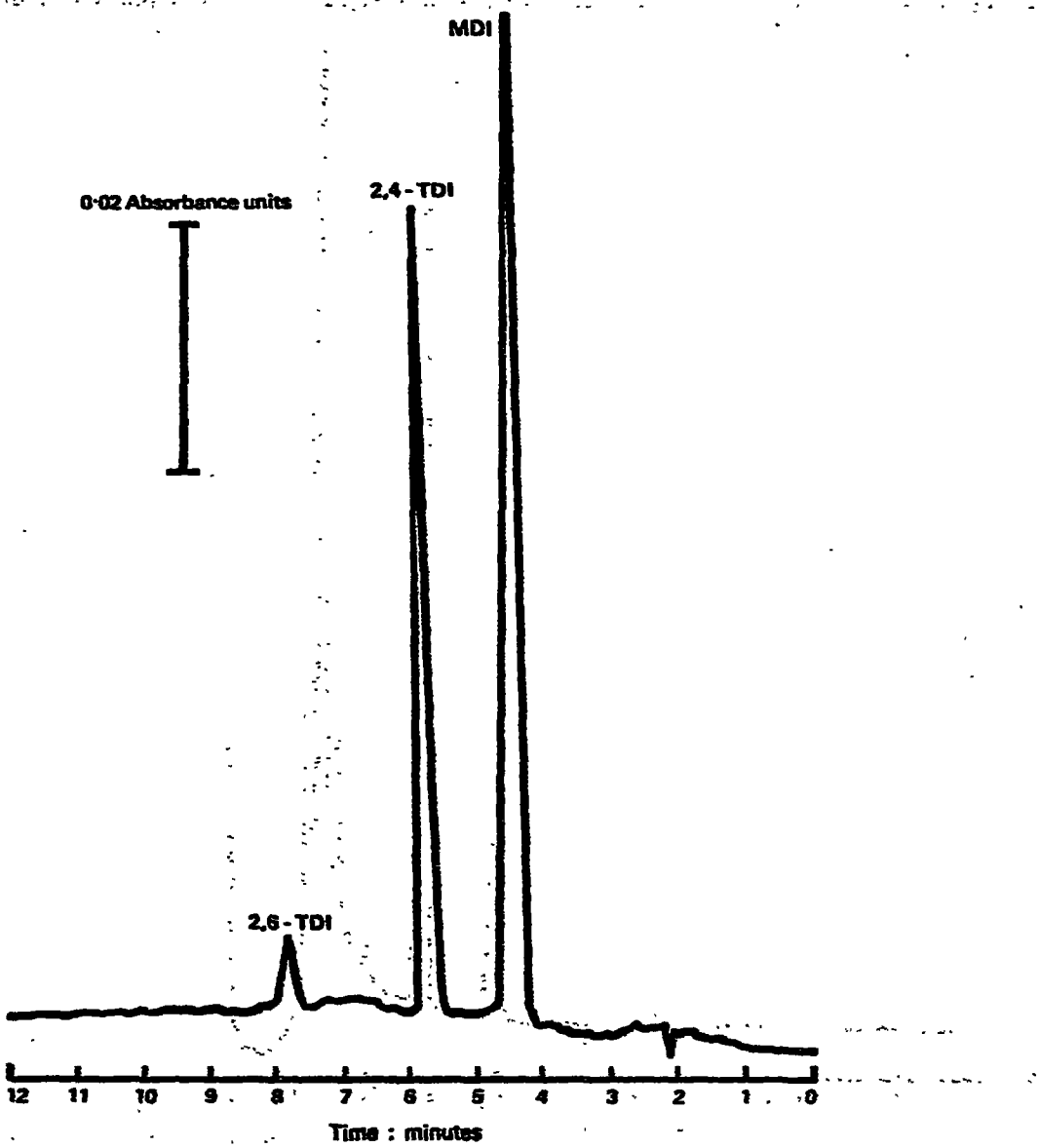

Fig. 4. Chromatogram of a TDI and MDI bulk sample. Conditions as in Fig. 1, except: mobile phase, methanol–dichloromethane (0.5:99.5); detection, 246 nm.

cases where isocyanates or isocyanate-containing products are used with particular reference to HDI prepolymers. We have experienced no problem with interferences from the range of solvents commonly used in isocyanate prepolymer products.

Ethanol reagent method for aromatic isocyanates in air (B)

Aromatic isocyanates react with ethanol to form strongly UV-absorbing ethyl urethane derivatives. Fig. 4 shows a chromatogram of TDI and MDI ethyl urethanes using the same column as for the nitro reagent method but with mobile phase B. Our

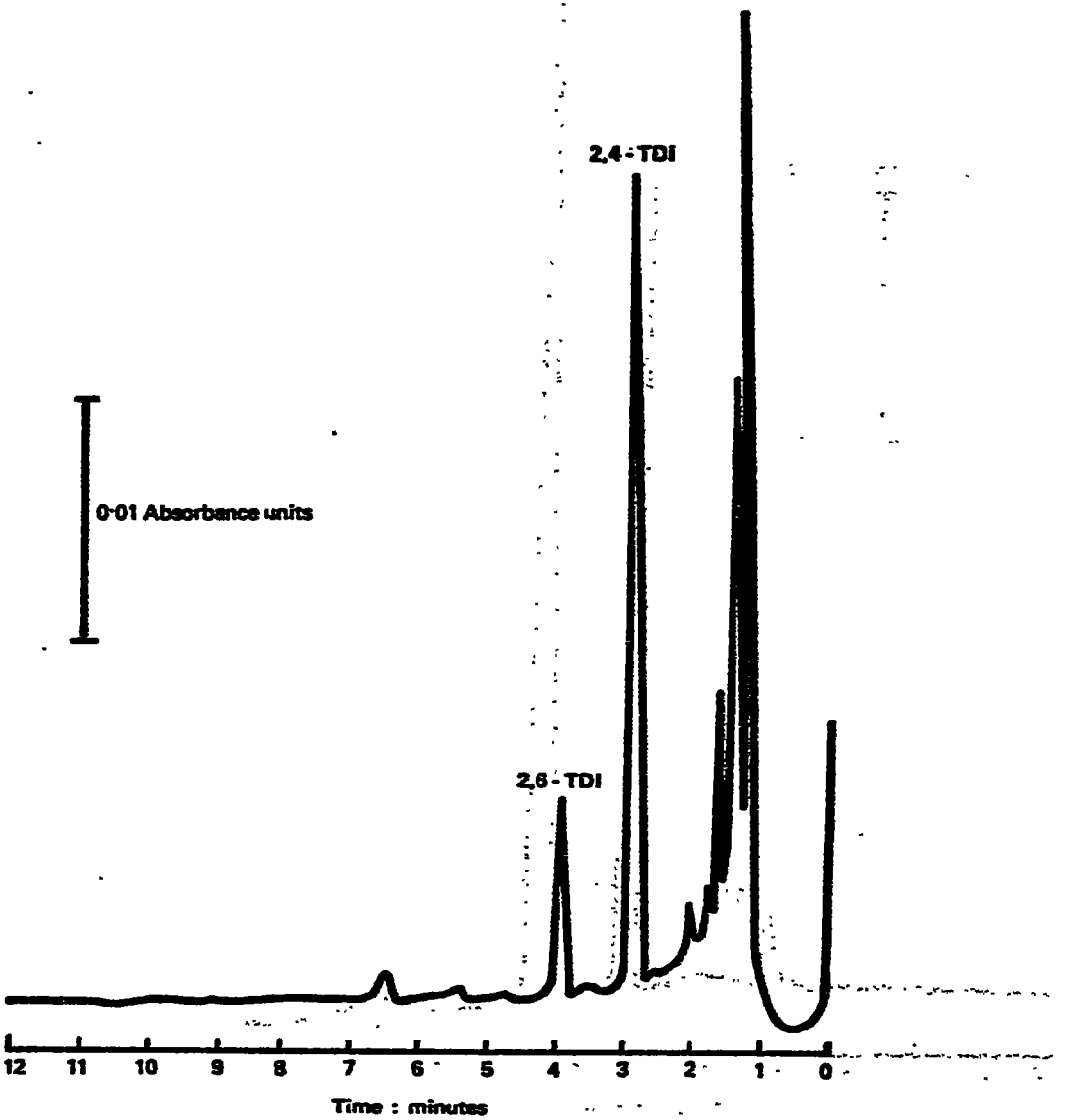

Fig. 5. Chromatogram of a TDI in air sample. Conditions as in Fig. 4, except: mobile phase, methanol–dichloromethane (0.75:99.25).

particular use of the ethanol reagent method has been primarily for the measurement of TDI and MDI in air. The collection efficiency of the method was checked and found to be 100%. Fig. 5 shows a chromatogram of a 15-l air sample containing TDI at a concentration of 70 $\mu g/m^3$. [This atmosphere was monitored independently by a UEI 7000 TDI monitor (MDA Scientific, Wimborne, Great Britain)]. Recovery for the method was 95% ± 5%.

The detection limits for the TDI and MDI ethyl urethanes for a 10-l air sample containing TDI and MDI absorbed into 10 ml of ethanol was 2 $\mu g/m^3$, this is five times more sensitive than the nitro reagent method (Table I) for these isocyanates.

Organic solvents contained in commercially available aromatic isocyanate prepolymers do not interfere with the analysis: evaporation of the ethanol–isocyanate

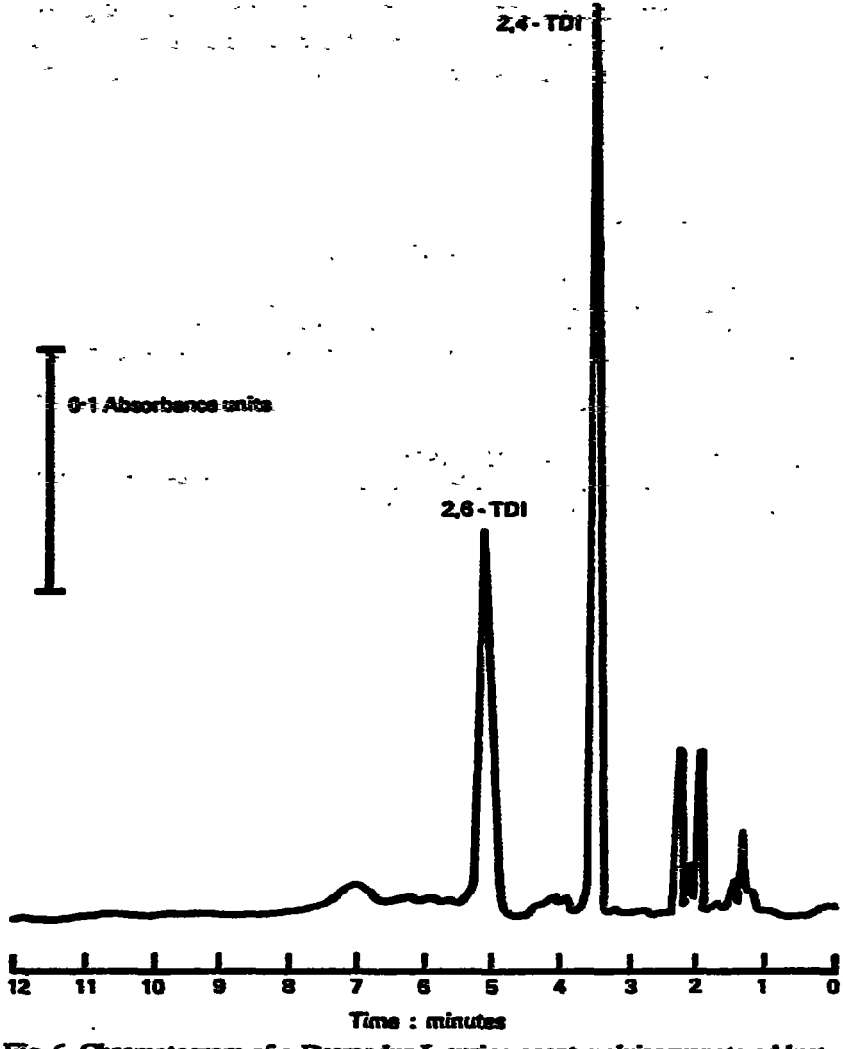

Fig. 6. Chromatogram of a Desmodur L curing agent–polyisocyanate adduct sample. Conditions as in Fig. 5, except: amount injected, 2 µl.

reaction mixture after sampling removes most of the organic compounds and others elute before the peaks of the isocyanate ethyl urethane derivatives. Fig. 6 shows the analysis of a sample of a Desmodur L curing agent–polyisocyanate adduct, which contained free isocyanate and other organic compounds.

CONCLUSION

The methods described here have been successfully used to measure free monomeric aliphatic and aromatic isocyanates in factory environments. The nitro reagent method has been improved by making the derivatisation of unreacted nitro reagent simpler, column life is extended and there is no need for gradient elution giving an effective reduction in sample analysis time. This method has been primarily used in this laboratory for the measurement of aliphatic isocyanates. Although the nitro reagent method may be used for the measurement of aromatic isocyanates, the ethanol reagent method is preferable since the detection limits attainable for these isocyanates are lower.

REFERENCES

1 K. Marcali, *Anal. Chem.*, 29 (1957) 552.
2 D. W. Meddle and R. W. Wood, *Analyst (London)*, 95 (1970) 402.
3 J. Keller, K. L. Dunlop and R. L. Sandridge, *Anal. Chem.*, 46 (1974) 1845.
4 K. L. Dunlop, R. L. Sandridge and J. Keller, *Anal. Chem.*, 48 (1976) 497.
5 C. R. Hastings Vogt, C. Y. Ko and T. R. Ryan, *J. Chromatogr.*, 134 (1977) 451.
6 P. Goldberg and P. A. Maddison, I.C.I. Organic Division, Blackley, Manchester, personal communication, 1978.
7 G. B. Cox, C. R. Loscombe, M. J. Shucutt, K. Sugden and J. A. Upfield, *J. Chromatogr.*, 117 (1976) 269.
8 D. A. Bagon and H. L. Hardy, *J. Chromatogr.*, 152 (1978) 560.
9 G. D. Nelson, *Controlled Test Atmospheres*, Ann Arbor Sci. Publ., Ann Arbor, Mich., 1971.
10 G. B. Cox and K. Sugden, *Anal. Chim. Acta*, 91 (1977) 365.