Journal of Chromatography, 346 (1985) 446–449
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 18 002

Note

Reversed-phase high-performance liquid chromatography of methyl isocyanate

C. D. RAGHUVEERAN* and M. P. KAUSHIK
Defence Research and Development Establishment, Tansen Road, Gwalior-474002, Madhya Pradesh (India)
(Received June 3rd, 1985)

Methyl isocyanate (MIC) is a toxic chemical intermediate like the other industrially used organic isocyanates. It has a high vapour pressure and due care should be exercised while working with this compound. High-performance liquid chromatographic (HPLC) methods are available for the determination of toluene diisocyanate (TDI), hexamethylene isocyanate (HMI), etc., but we believe that so far no HPLC procedure has been described for MIC. The above methods depend on the conversion of the isocyanates into more stable, UV-absorbing[1,2] or fluorescing[3] urea derivatives by use of suitable primary or secondary amines.

We report here a reversed-phase HPLC procedure for the determination of MIC by reaction with a readily available aromatic amine to form a urea derivative absorbing at 254 nm. The method is sensitive to nanogram quantities of MIC.

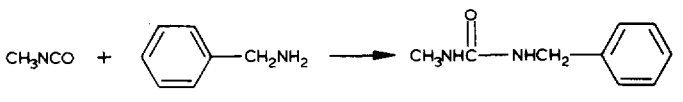
EXPERIMENTAL

Equipment

The liquid chromatograph used was assembled from the following components: an SP-8750 ternary solvent delivery system (Spectra-Physics, U.S.A.) equipped with a Rheodyne Model 7125 injector and a 10-μl loop; a PRP-1 column (Hamilton, Bonaduz, Switzerland) packed with styrene–divinylbenzene (10 μm, 150 × 4.1 mm); an SF-773 variable-wavelength detector (Kratos Analytical, U.S.A.) operated at 254 nm; a C-R1B Chromatopac data processor (Shimadzu, Japan). The chromatograph was operated in isocratic mode.

Chemicals

MIC was prepared in our laboratory by refluxing acetyl chloride with sodium azide in the presence of a phase-transfer catalyst[4]. It was distilled, collected in a chilled receiver and characterized by spectroscopic techniques. Benzylamine (Riedel), distilled with zinc dust, was used for derivatizing MIC into N-benzyl-N′-methylurea (BMU) according to the reaction:



0021-9673/85/$03.30

The structure and purity of BMU synthesized as above were established by elemental and spectroscopic (IR, ^{1}H NMR and electron impact mass spectrometry) analysis. This substance served as a reference for the identification of MIC. Quantitation was, however, achieved by forming BMU *in situ* in aqueous methanol containing benzylamine.

The solvents used for the mobile phase were methanol (guaranteed reagent; E. Merck, India) and water, distilled in an all-glass triple distillation apparatus. The two solvents were mixed in the proportion 90:10 together with 0.0025% perchloric acid, and filtered over a Millipore filtration system.

Procedure for BMU in situ

About 0.2 ml of MIC were accurately weighed and dissolved in a solution of benzylamine in the eluent used for LC*. The molar concentration of the amine was always in excess of that of MIC to ensure an adequate concentration for the formation of BMU. The ratio of the concentrations of MIC to benzylamine was 1:1.5. This solution served as a stock solution.

The precautions taken while preparing this stock solution were as follows: (i) MIC was weighed in a leak-proof container (a 10-ml graduated stoppered test-tube, with a quickfit stopper kept in place by a thin film of silicone grease; (ii) MIC weighed as above was kept chilled in an ice-bath till dissolution in the amine solution; (iii) the benzylamine solution was also chilled before mixing with MIC. This procedure was adopted so as to minimize the loss of MIC during the *in situ* reaction and to maximize the trapping of the substance in the bulk of the solution.

Working standards in the range 0.01–0.1 μg (10–100 ng) were made by serial dilution in methanol. A 10-μl volume of each standard was injected into the column.

RESULTS AND DISCUSSION

The *in situ* generation of BMU has been devised with a view to using a solution of benzylamine as a trapping fluid for MIC in the atmosphere. Other isocyanates are usually trapped in toluene containing an amine. The solvent is removed by evaporation and the residue is reconstituted in the eluents to be employed for reversed-phase HPLC[5]. In the procedure described here, the amine solution containing BMU can be injected into the column after suitable dilution in the mobile phase. Thus losses during the sample work-up can be minimized.

BMU is eluted at 1.75 min under the chromatographic conditions described. Fig. 1 shows a chromatogram of the synthesized BMU. In the *in situ* process (Fig. 2), the corresponding chromatogram contains a peak for the unreacted benzylamine (peak 1) which is eluted before BMU. The amine peak is sharp due to the presence of perchloric acid in the mobile phase. Fig. 3 shows a chromatogram of a benzylamine solution intended for trapping MIC and suitably diluted before the injection.

A calibration for MIC was performed according to the procedure described in the Experimental. An aliquot of the stock solution of BMU equivalent to 100 mg of MIC was diluted in methanol so as to give a concentration equivalent to 10 mg/ml of MIC. The calibration curve was plotted on the basis that 2.8 parts by weight of

* MIC is highly volatile. Measuring out accurate volumes of it was rendered difficult due to high ambient temperatures.

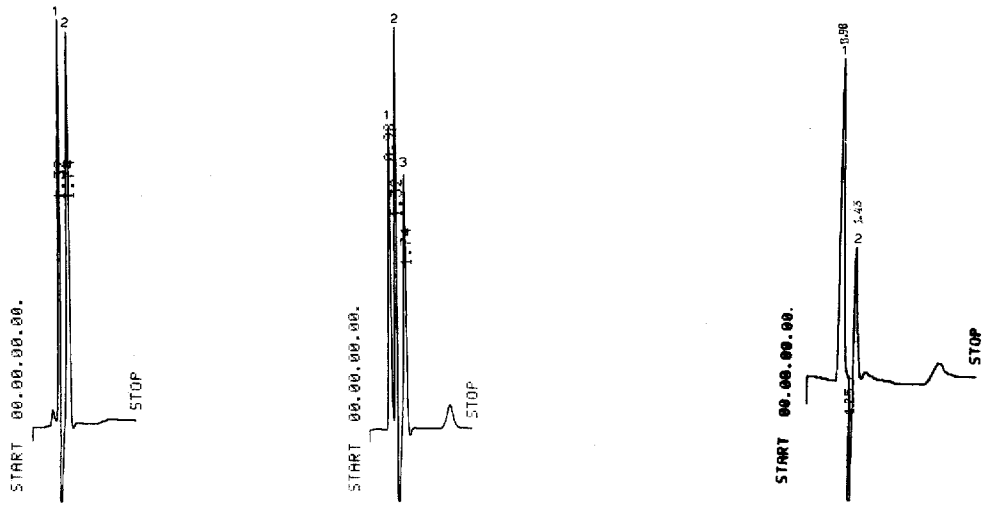


Fig. 1. Chromatogram of synthesized BMU. Conditions column, PRP-1; eluent, methanol–water (90:10) containing 0.0025% perchloric acid; flow-rate, 1 ml/min; sample size, 10 μl; detection, UV, 254 nm, 0.01 a.u.f.s., C-R1B attenuation 2. Peaks: 1 = unknown (from methanol); 2 = BMU.

Fig. 2. Detection of MIC as BMU *in situ*. Conditions as in Fig. 1. Peaks: 1 = benzylamine; 2 = unknown (from methanol); 3 = MIC (60 ng).

Fig. 3. Benzylamine injected as a blank. Conditions as in Fig. 1. Peaks: 1 = benzylamine (diluted); 2 = unknown (from methanol).

BMU are equal to 1 part by weight of MIC. The working standards were made from this solution by dilution in methanol. A plot of the concentration of MIC (0.01–0.1 μg) *versus* peak height is linear (Fig. 4). Such a calibration plot can be useful for monitoring MIC in the atmosphere.

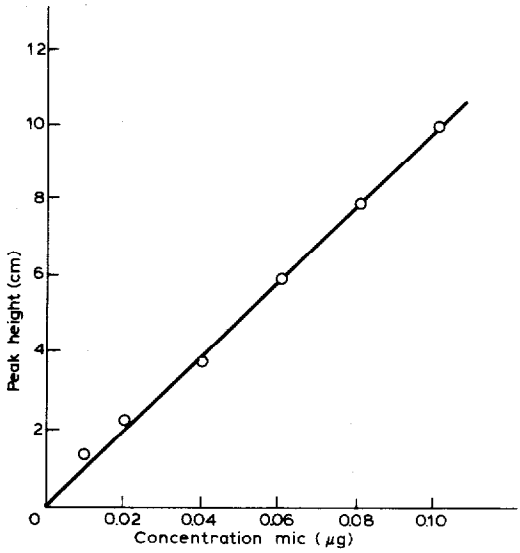


Fig. 4. Calibration plot for MIC.

The choice of the solvent for the amine reagent was based on experiments with water, methanol, acetonitrile and methanol–water (90:10) (with and without perchloric acid). Standards of BMU of identical concentration were injected in each of these solvents and the peak heights compared. Only water–methanol (80:20), acetonitrile and methanol–water (90:10) containing perchloric acid, *i.e.*, the mobile phase, gave linear calibration plots. The data are presented in Table I from which it is evident that the mobile phase is the best medium for preparing the amine reagent.

TABLE I

CHOICE OF SOLVENT FOR BENZYLAMINE

Concentration of MIC: 10 ng; sensitivity setting: 0.01 a.u.f.s.; recorder setting (C-R1B): attenuation 2.

Solvent	*Peak height of MIC (cm)*
(1) Water–methanol (80:20)	5.5
(2) Acetonitrile	6.8
(3) Methanol–water (90:10) containing 0.0025% perchloric acid	7.5

CONCLUSION

A reversed-phase HPLC procedure has been developed which makes use of a commonly available reagent, *viz.*, benzylamine, for derivatizing MIC into a urea derivative detected at 254 nm. The method is linear in the range 0.01–0.1 μg (10–100 ng) MIC. For trapping MIC from sources like air and water, the benzylamine solution can be prepared in the mobile phase. Work is in progress to utilize the technique for air monitoring.

ACKNOWLEDGEMENT

We thank Dr. P. K. Ramachandran, Director, Defence Research & Development Establishment, Gwalior for active encouragment and guidance.

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