Failure Report No. S252

May 11, 1979

Substance: Methyl Isocyanate

OSHA Standard: 0.02 ppm (0.05 mg/cu m)

Chemical Used: Methyl Isocyanate, Eastman Chemical

Methods Attempted

The method developed by Levine et al., (Reference 1) was modified for use as a sampling and analysis method for methyl isocyanate. The method evaluated involved coating XAD-2 resin with 1-naphthylene-methylamine (NMA), collecting methyl isocyanate which reacts with NMA to form a fluorescent derivative, followed by desorption with toluene and analysis by HPLC with a fluorescence detector.

The use of N-4-nitrobenzyl-N-n-propylamine was also evaluated as a derivatizing reagent (Reference 2). The analysis in this case was performed using HPLC but utilized an ultraviolet absorbance detector.

Reason for Failure

The methods evaluated had various problems, several of which were common to both. The principal problems were;

1. Slow reaction times in solvents that could be used.

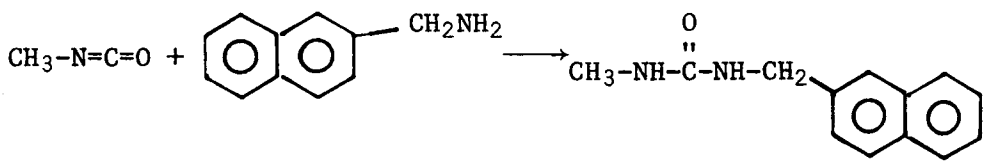
2. Instability of derivatizing reagents.

The instability of the derivatizing reagents was the cause of several other problems with both methods. The difficulties encountered with both analytical methods is discussed in detail below.

Discussion

1. HPLC - Fluorescence Method

The HPLC/fluorescence method is based on the reaction of naphthylene-methylamine (NMA) with methyl isocyanate:



As indicated in the literature (Reference 1), methyl isocyanate is collected by trapping in a solution of NMA in toluene contained in a midget impinger. Due to the flammability of toluene, this sample

collection method could not be utilized in this program. Method development work then proceeded on the premise that a solid sorbent of some type would be used to collect methyl isocyanate. Calibration solutions in toluene were prepared and chromatographic conditions for the analysis were then determined.

The following conditions were found to be adequate for the analysis of the methyl isocyanate - NMA derivative.

1. Column: MicroBondapakCN
2. Mobile Phase: 30/70 Acetonitrile/Water
3. Flow: 1.5 mL/min
4. System Pressure: 1000 psi
5. Excitation Wavelength: 216 nm
6. Emission Filter: 370 nm
7. Time Constant: 7 sec.
8. Sensitivity: 568
9. Range: 1.0 μA

The equipment used for this analysis included two Waters Associates Chromatography pumps, a Waters Model 660 Solvent Programmer, a Waters Model 440 UV Absorbance Detector, a Waters Model U6K Injector, a Schoeffel FS970 LC Fluorometer and a Spectra Physics Integrator.

Initial experiments were carried out using toluene and acetonitrile as solvents. A single standard in each solvent was continually injected to determine the time needed for completion of the reaction. The use of toluene as a solvent resulted in large negative responses after the sample peak. Alternate emission filters (390, 418 nm) were used in an attempt to remove this response but these were inadequate and also resulted in decreased sensitivity. Use of acetonitrile eliminated this problem, but the rate of reaction appeared much slower, with at least three hours needed for completion. In subsequent, more controlled time studies, however, it was discovered that the reaction proceeded at similar rates in both solvents. There was no apparent advantage to using toluene so that a series of standards was prepared as follows:

a. A 10^{-4} M NMA solution was prepared using acetonitrile as the solvent.

b. Under nitrogen, a stock solution of methyl isocyanate was prepared by adding 5 μL of pure methyl isocyanate to 10 mL of acetonitrile.

c. Calibration standards were prepared at concentrations of 0.097, 1.2 and 2.4 μg/mL by injecting appropriate aliquots of the stock solution into 10^{-4} M NMA in acetonitrile.

d. The calibration standards were allowed to stand at room temperature overnight to ensure complete reaction.

e. Replicate injections of each standard were then made the following morning.

The resulting calibration curve was quite acceptable as can be seen in Figure S252-1. It should be noted here that the analytical grade methyl isocyanate was stored in septum-capped vials. The vials were placed in a desiccator and the desiccator was kept under nitrogen.

A batch of XAD-2 was treated with an alcoholic NMA solution, dried under vacuum and analyzed for NMA content. A 1.7% loading was calculated; therefore 1.7 mg of NMA would be available to collect methyl isocyanate with 100 mg of treated XAD-2. This represents a 130-fold molar excess of NMA when methyl isocyanate is collected for 4 hours at 0.2 liter per minute at twice the OSHA standard. Considering that other isocyanates may be present as well as water, this is not an extremely large excess.

A 100-mg portion of NMA-treated XAD-2 was extracted with 1 mL of acetonitrile. The extract was analyzed by HPLC with fluorescence detection. The chromatogram is given in Figure S252-2. For comparison, the chromatogram of a standard is given. Note that one of the major peaks in the blank sample coelutes with the sample peak. A separate analysis of untreated XAD-2 showed no peaks whatsoever, indicating that the presence of NMA was the cause of the situation.

In order to confirm that NMA was the cause of the problem, two other solid sorbents were tested. These were Chromosorb 104 and Tenax-GC. Tenax-GC showed 9 peaks and Chromosorb 104, 17 peaks. At this point, it was clear that while NMA had to be present for these peaks to appear, all sorbents tested did not show similar behavior. In order to isolate what part NMA played, a similar aliquot of the solution used to treat the solid sorbents was placed in an evaporating dish. The solution was allowed to evaporate under nitrogen. The residue was then dissolved in acetonitrile and a portion of this solution was injected. Seven peaks appeared in the chromatogram. In every case where blanks were analyzed, an interfering peak was observed.

The remaining hope in applying the basic analytical method laid in the possibility that a solution of NMA in a non-flammable solvent could be added to the sorbent after collection. This would convert the methyl isocyanate to a stable form. Several chlorinated hydrocarbons were injected to see what effect they might have on chromatography. Methylene chloride and carbon tetrachloride were found to have a serious effect on the baseline. Ethylene glycol was tested for application as a solvent as well. No chromatographic interferences resulted, but the reaction did not appear to proceed to completion. Peak heights of the methyl isocyanate-NMA derivative in ethylene glycol were 20% of those in either toluene or acetonitrile. With the combination of results achieved thus far work was discontinued on this analytical method.

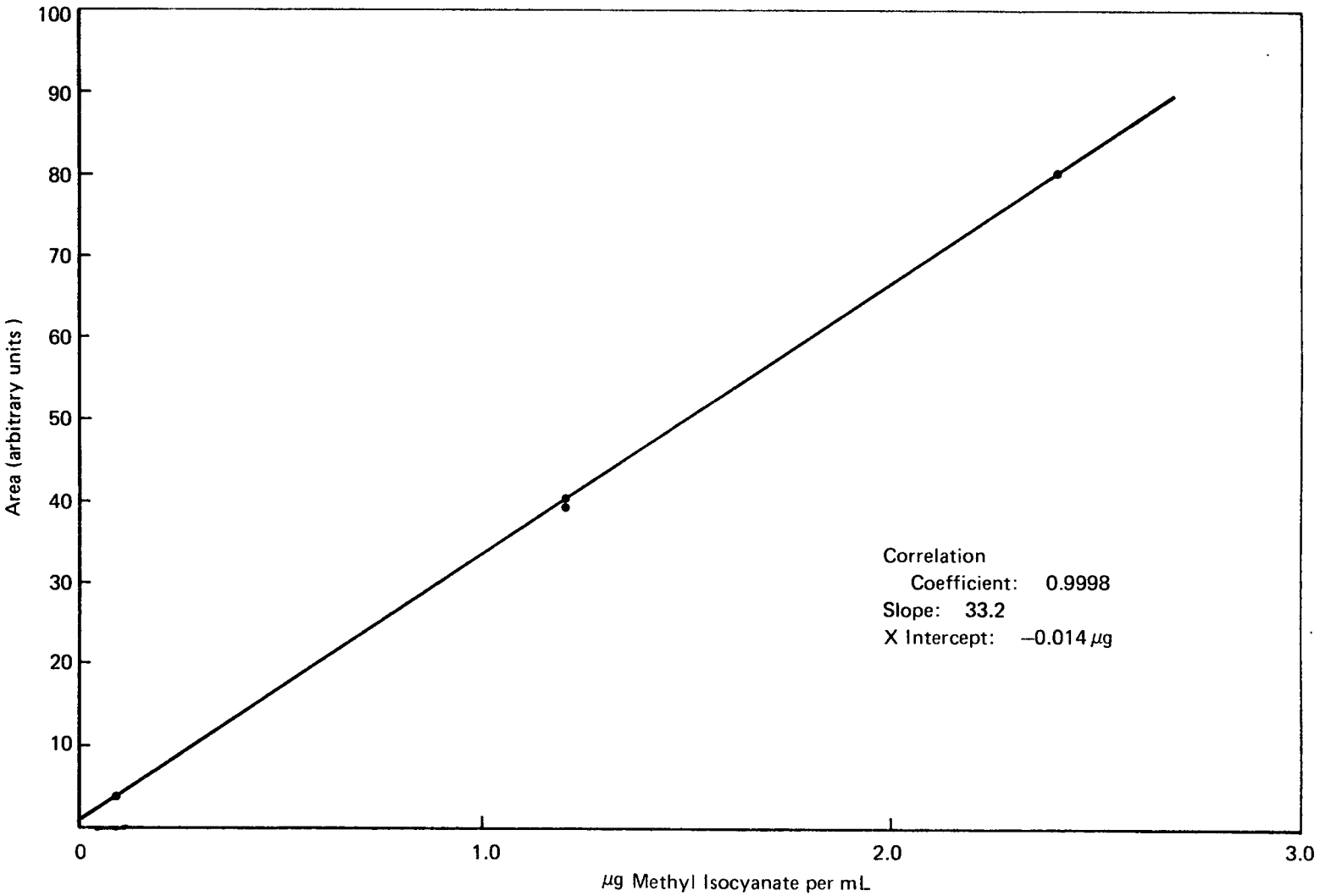


FIGURE S252–1 CALIBRATION CURVE FOR METHYL ISOCYANATE AS NMA DERIVATIVE

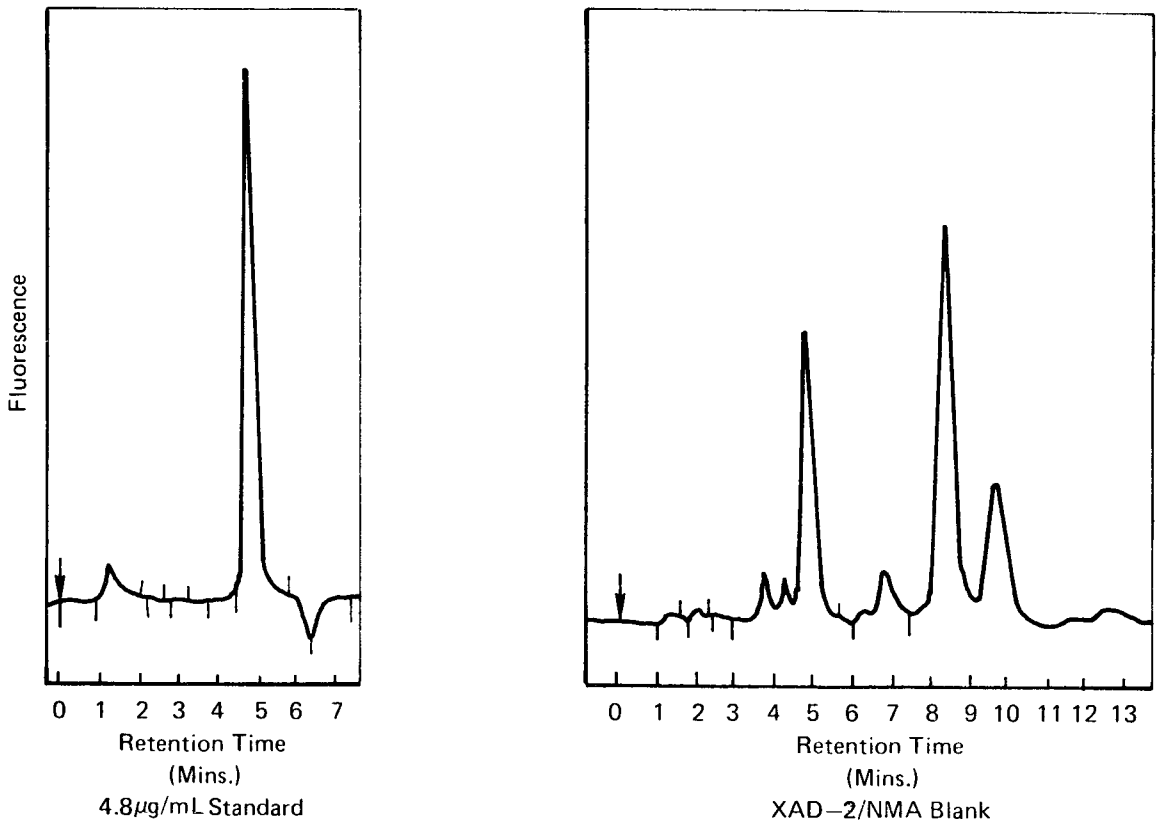


FIGURE S252–2 COMPARISON OF STANDARD AND BLANK CHROMATOGRAMS FOR PROPOSED METHYL ISOCYANATE–NMA METHOD

2. HPLC - UV Absorbance Method

In view of the results obtained for the fluorescence method, the investigation of the Nitro Reagent method (Reference 2) was conducted based on the premise that in situ reaction would be difficult at best. As a result, experiments were designed to evaluate the feasibility of using the Nitro Reagent solution to stabilize methyl isocyanate. In view of previous problems associated with excess Nitro Reagent (Reference 2), standards were prepared by adding aliquots of methyl isocyanate stock standard to 1 mL of 2×10^{-4} M Nitro Reagent. For a 48-liter sample at the OSHA standard level 2.4 µg or 4.2×10^{-8} moles of methyl isocyanate is collected. If desorbed with 1 mL of 2×10^{-4} M Nitro Reagent in methylene chloride there will be an excess of a factor of five in favor of the Nitro Reagent. This was done to minimize problems of column deterioration associated with the Nitro Reagent. In spite of this, several problems were encountered with the chromatography and as a result several systems were evaluated.

Initially, promising results were achieved using a MicroBondapak CN column and methylene chloride as the mobile phase. Separation between the sample peak and excess Nitro Reagent was adequate in spite of obvious tailing problems. The analysis, however, was plagued by several inconsistencies. The most confusing event was that the number of peaks that appeared for identical solutions changed from day to day. Also, it appears that the reaction is not instantaneous. In a time study of calibration solutions, peak heights had not stopped increasing after two hours.

3. GC/AFID - Independent Method

In efforts to develop an independent method of analysis, a third analysis technique was evaluated--gas chromatography. The equipment used was a Hewlett-Packard Model 5840A gas chromatograph equipped with a nitrogen/phosphorus flame ionization detector and a 6' x 2 mm I.D. glass column packed with 10% SP1000 on 100/120 Supelcoport.

The chromatographic conditions were as follows:

1. Column Temperature: 50°C
2. Injector Temperature: 100°C
3. Detector Temperature: 150°C
4. Carrier (He) Flow: 30 mL/min
5. Air to Detector: 50 mL/min
6. H_2 to Detector: 3 mL/min

Six 100-mg portions of XAD-2 were spiked with 2.4 µg of methyl isocyanate and left overnight. An average of 60% was recovered, meaning that methyl isocyanate collected on untreated sorbent must be put into solution immediately after collection. Spikes desorbed within an hour showed 86% recovery. Non-flammable solvents such as methylene chloride and carbon tetrachloride could not be used since they are not compatible

with the detector used, so that use of this method appears to be limited to cases where the sample need not be shipped or to use in the laboratory as an independent method.

Conclusions

The rate of reaction between methyl isocyanate and either NMA or the Nitro Reagent does not appear to be rapid enough to work as a collection method. The use of the Nitro Reagent also appears to have an adverse effect on the analytical method in that very broad, tailing peaks result in extended analysis time. NMA on the other hand, had introduced no complications in this regard. Its use as an *in situ* reagent appears limited, however, due to the large number of peaks observed for sorbent blanks. Analysis of NMA standards showed much more than adequate sensitivity as well as sufficient reproducibility, given that the reaction was complete. In the HPLC/UV method, sensitivity is much reduced for the Nitro Reagent/methyl isocyanate derivative, in fact it is barely sufficient to detect 5% breakthrough for a 4-hour sample.

Recommendations

The HPLC-Fluorescence method is clearly the superior analytical method in terms of reproducibility, sensitivity and chromatographic consistency. It is recommended, however, that a substitute be found for naphthylenemethylamine as a derivatizing reagent. A more stable compound is needed for elimination of interfering peaks associated with NMA. If such a compound could be found, then the method may stand a good chance of being validated. A compound which has the amine group more removed from the aromatic portion of the molecule such as naphthylene ethylamine may be a good starting point. Careful attention should be paid to the stability of the reactant, both in solution and when exposed to air.

References

1. Levine, S.P., *et al.*, *Anal. Chem.* *51* (8), 1106-1109 (1979).

2. 2,4-Toluenediisocyanate (TDI) Failure Report No. S344, prepared under NIOSH Contract No. 210-76-0123.