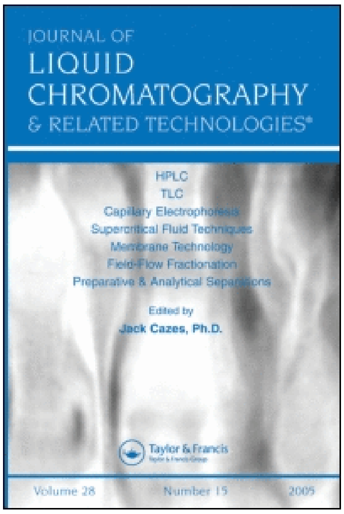

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COLLECTION AND CHEMICAL DERIVATIZATION OF AIRBORNE PHOSGENE WITH 1-(2-PYRIDYL)-PIPERAZINE AND DETERMINATION BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

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ABSTRACT

As an alternative to currently available measurement methods, Chromosorb coated with 1-(2-pyridyl)-piperazine (PYP) was evaluated for collection / derivatization of phosgene gas. Solid sorbent tubes contained 100 mg of 2.5% PYP coated on Chromosorb. Phosgene reacts with two equivalents of PYP to form a substituted urea derivative which is desorbed with acetonitrile and determined by reversed phase high performance liquid chromatography with ultraviolet absorbance detection. In comparison to the 4,4'-nitrobenzyl pyridine in diethylphthalate colorimetric technique, the recovery of phosgene from the sorbent tube was quantitative from 0.02 to 1 ppm phosgene and was unaffected by humidity. The limit of detection for a 20 L air sample was estimated to be 0.005 ppm. The utility of the method was further improved by demonstrating the use of triphosgene [bis-(trichloromethyl)-carbonate] in the synthesis of the urea derivative used for standardization, thus eliminating the need for working with gaseous phosgene in preparing analytical standards.

INTRODUCTION

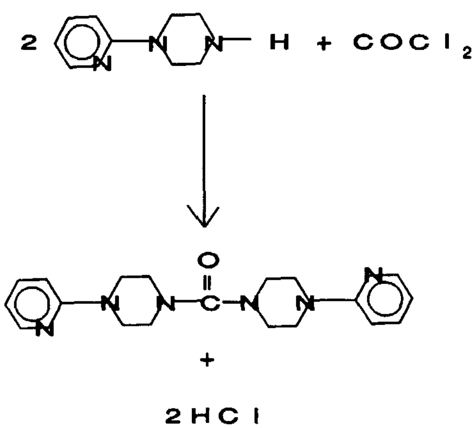
Phosgene ($COCl_2$) is a highly toxic chemical intermediate used primarily for industrial production of isocyanates and polycarbonates. Surreptitious exposure to phosgene may also occur through decomposition of vapors of chlorinated hydrocarbons under the influence of ultraviolet light. In 1983, it was estimated that 2358 workers were exposed to phosgene in the Unites States.[1] Exposure to concentration of 3 to 5 ppm causes irritation of the eyes and throat, while 25 ppm is dangerous for exposures of 30 to 60 minute duration and may result in delayed onset of pulmonary edema.[2] The current allowable exposure level in the United States is 0.1 ppm (0.4 mg/m^3) as an 8-hour time weighted average.[3]

The sampling and analytical method for determining phosgene in air recommended by the National Institute for Occupational Safety and Health (NIOSH) employs a midget impinger containing a solution of 0.25% 4-(4'-nitrobenzyl)-pyridine and 0.5% N-phenylbenzylamine in diethylphthalate.[4] Phosgene in air reacts with the solution to produce a brilliant red color which can be measured spectrophotometrically at 475 nm. This method was originally described by Lamouroux,[5] and later modified and improved by other investigators.[6,7] However the technique has the following deficiencies: (1) the color formed is unstable and a 10 to 15% decay is reported after 8 hours of storage;[8] (2) water vapor interferes with the measurement with an 11% reduction in color intensity observed at 73% relative humidity;[7] and (3) the use of impingers in the field has the potential of spillage of solution, breakage of glassware, and contamination with diethylphthalate.

Phosgene generally reacts with primary and secondary amines to form substituted urea derivatives. For example, aniline has been used to convert phosgene to N,N'-diphenylurea for quantitative measurement by either gravimetry[9] or spectrophotometry.[10,11] While modern chromatographic procedures could be utilized to overcome lack of specificity and sensitivity of these gravimetric or spectrophotometric analyses, the use of a primary amine like aniline can result in a mixture of polysubstituted urea compounds with phosgene, making the chromatographic approach less reliable.

Certain secondary amine compounds are commonly used for chemical derivatization of isocyanates which, like phosgene, form substituted urea compounds amenable to chromatographic determination. One of the most common of these reagents is 1-(2-pyridyl)-piperazine [PYP]. PYP reacts on a one to one basis with isocyanate compounds yielding a stable urea derivative which can be quantitated specifically and sensitively with reversed phase, high performance liquid chromatography and ultraviolet absorbance detection.[12,13]

The use of a single derivatizing agent for chromatographic determination of both isocyanates and phosgene would be of particular benefit since these materials are usually encountered together in isocyanate manufacturing facilities. Therefore this work was directed at adapting the PYP method for isocyanates to the measurement of phosgene in air. PYP reacts with phosgene as follows:



The PYP urea derivative exhibits a unique chemical structure and is amenable to chromatographic separation and ultraviolet absorbance detection. Based on this, the PYP sampling technique has been modified for collection of phosgene on a coated solid sorbent.[14] Phosgene is converted to the PYP urea derivative on the sorbent, subsequently solvent desorbed, and determined by HPLC. This work presents the results of the development and evaluation of the technique.

In addition, the use of triphosgene [bis-(trichloromethyl)-carbonate] as a surrogate standard for phosgene is explored as a suitable safe alternative to handling of phosgene gas. Triphosgene has been successfully used as a substitute for phosgene in various organic syntheses.[15,16] In general, reactions require one-third equivalent of triphosgene in comparison to phosgene. Reaction products of triphosgene with compounds containing labile hydrogen are usually identical to those obtained from phosgene. The great advantage of triphosgene is that the material is a stable, crystalline solid (M.P. 81-83°C), making it safer and more convenient to handle than phosgene. However it should be noted that under certain conditions, triphosgene has been noted to release significant amounts of phosgene.[17] In this work, triphosgene was utilized for preparation of standards for spectrophotometric and liquid chromatographic determination of phosgene.

MATERIALS AND METHODS

Pure phosgene (99%) was obtained as the liquified, compressed gas from Matheson Gas Products (Secaucus, New Jersey). Triphosgene was obtained as the crystalline material, 98% purity, from Aldrich (Milwaukee, Wisconsin). 1-(2-Pyridyl)-piperazine, 98%, was also obtained from Aldrich. Chromosorb W, acid washed, 80/100 mesh was supplied by Alltech Associates Inc. (Deerfield, Illinois).

Synthesis of Phosgene-PYP Urea

The urea derivative of phosgene and PYP was prepared in the laboratory as follows: phosgene gas from a compressed gas cylinder was directed into a cold trap at ice bath temperature and allowed to liquify; 125 μL of liquid phosgene was dissolved in 5 mL of acetone at 0°C; the phosgene / acetone solution was slowly added with stirring to a solution of 1 mL PYP in 50 mL distilled water, also at 0°C; the resulting solution was allowed to warm to room temperature over a period of about 30 minutes. The PYP-phosgene-urea separated from solution as a white precipitate. This was collected in a Büchner funnel, thoroughly dried, and then recrystallized out of hot toluene. Alternatively, triphosgene was substituted for phosgene in the synthesis. In this case, 125 mg of solid triphosgene was used in place of the liquid phosgene.

The identities of the derivatives were confirmed by elemental analysis and infrared spectroscopy. Typical results of elemental analysis were as follows: expected composition, C:64.75%, H:6.81%, N:23.84%, O:4.54%; found, C:65.06%, H:6.76%, N:24.02%, O:5.31%. Infrared spectroscopy showed a band at about 1625 cm^{-1}, corresponding to the urea carbonyl stretch. No evidence of free amine (N-H stretching frequencies) was observed in the spectrograms. The urea derivatives prepared from phosgene and triphosgene appeared identical by elemental analysis, infrared spectroscopy, and HPLC. The molar absorptivity of the derivative in methanol was found to be 3.52 x 10^4 L-$mole^{-1}$-cm^{-1} at 254 nm.

Phosgene Test Atmospheres

Test atmospheres of phosgene were produced in a dynamic flow-through manifold constructed from pyrex glass tubing. Phosgene gas was generated from a calibrated, standard permeation tube, 2.5 cm in length (VICI Metronics, Santa Clara, California) which was maintained at a constant temperature of 30°C. The tube was weighed periodically on a Mettler H51AR analytical balance to establish its gravimetric output. The output from the permeation tube was diluted with dry air and then mixed with dilution air from a humidifier/dehumidifier system. The diluted test atmosphere then passed into the sampling manifold and out through the exhaust. The total flow through the system ranged from 4 to 20 L per min, depending on the desired phosgene concentration.

Concentration of phosgene in the test atmospheres was established either by calculation from the gravimetric output of the permeation tube and the flow through the system, or by direct determination with the colorimetric technique of NIOSH. The former approach was used only for dry test atmospheres.

According to the NIOSH technique,[4] standardization is accomplished by sampling known amounts of gaseous phosgene from a calibrated permeation tube or other standardized test atmosphere. This approach requires set-up of a relatively complex apparatus with exacting control of phosgene output and dilution flows. Additionally, gaseous phosgene has to be handled, resulting in certain safety and health considerations. In order to circumvent these problems, we evaluated the use of triphosgene as a surrogate standard for the colorimetric analysis of phosgene as well.

Standards were prepared in solutions of 0.25% 4-(4'-nitrobenzyl)-pyridine and 0.5% N-phenylbenzylamine in diethylphthalate. For standardization according to the NIOSH protocol,[4] impingers containing 10 mL of the absorbing solution were used to sample dry test atmospheres of phosgene produced via permeation tube. Samples were collected at 0.5 L per min with the total sample volume varying between 0.5 and 30 L to obtain a full range of standard solutions (0.2 to 11.2 μg/mL). The amount of phosgene in the standards was calculated from the gravimetric output of the permeation tube, dilution flow rate through the system, and air sample volume. The absorbance of the standards was measured at 475 nm on a Perkin Elmer Lambda-1 spectrophotometer with 1 cm quartz cells.

Stock solutions of triphosgene equivalent to 1 mg phosgene per mL were prepared by dissolving 50 mg of triphosgene in 50 mL of solvent. Diethylphthalate and hexane were separately evaluated as solvents. In either case, stock solutions were micropipetted into absorbing solutions to produce standards in the same range as those obtained directly from phosgene test atmospheres. To ensure proper mixing in the viscous diethylphthalate solution, samples were placed on a vortex mixer during standard additions.

Preparation and Use of PYP Sorbent Tubes

Ten g of Chromosorb was mixed with 10 mL of a solution of 2.5 % w/v PYP in hexane. The hexane was evaporated from the mixture under a nitrogen flow. The coated Chromosorb was brought to dryness visually under the nitrogen flow. Ten g of silanized glass wool was treated in the same manner. Glass tubes, 6.5 mm i.d. and 7.5 cm long, were packed with 100 mg of PYP coated Chromosorb. The packing was held in place with small plugs of PYP coated glass wool at each end.

Samples were collected by pulling air through the sorbent tubes at a rate of 1 L per minute. At this flow rate, a pressure drop of 0.30 inches Hg was noted across the tube. A total sample volume of at least 20 L is recommended. After collection, the glass wool and Chromosorb were quantitatively transferred to a development vial and desorbed with 1.0 or 2.0 mL acetonitrile with sonication for 10 minutes. Recovery of PYP-phosgene-urea from the sorbent tubes was found to be complete. Prior to HPLC analysis, the samples were filtered through a 0.45 μm pore Nylon syringe filter (Alltech Associates).

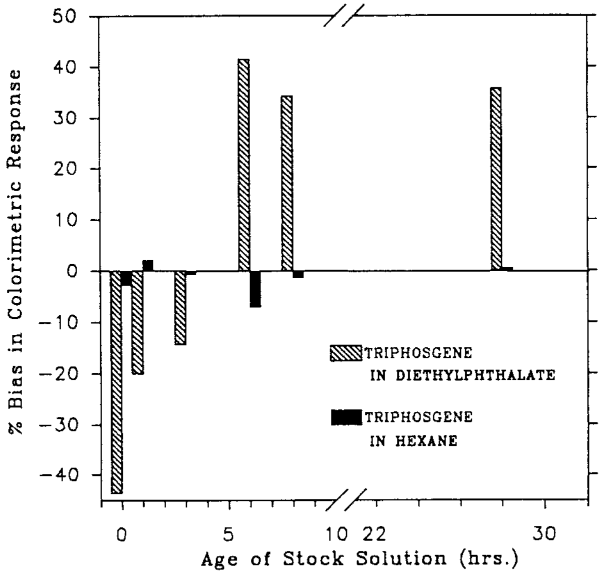


FIGURE 1 Effect of solvent on performance of triphosgene stock solution for standardization of spectrophotometric determination of phosgene. Percentage bias calculated in reference to authentic phosgene standards.

Chromatographic Determination of Phosgene Derivative

Samples were analyzed on a Perkin Elmer Model 410 high pressure liquid chromatograph. Peak Detection was accomplished by ultraviolet absorption with a Perkin Elmer Model LC90 UV detector set at a wavelength of 270 nm and with a Perkin Elmer Model 15B UV detector with a fixed wavelength of 254 nm. Samples were injected on-column with a Rheodyne injection valve. Injection volumes were 20 μL using a Pressure-Lok syringe (Precision Sampling Corp., Baton Rouge, Louisiana). Samples were chromatographed on a Supelcosil LC18-DB octadecyl bonded phase column, 5 μm particle size (Supelco, Belafonte, PA). Column dimensions were 5 mm i.d. x 25 cm long. The mobile phase consisted of acetonitrile / aqueous ammonium acetate buffer (3% NH_4OAc, adjusted to pH 6.0), and was pumped through the column at a flow rate of 1.5 mL per min. For routine analysis of phosgene-PYP-urea, 45% acetonitrile and 55% buffer was used. The chromatograms were recorded and peaks integrated with a Spectra Physics Model 4290 chromatographic integrator. Standards for the analysis were prepared by dilution of a stock solution of phosgene- or triphosgene-PYP-urea derivative in acetonitrile.

RESULTS AND DISCUSSION

Colorimetric analysis

Figure 1 shows the results of a comparison of the triphosgene standards to those obtained using gaseous phosgene for the colorimetric reference technique. A clear bias is observed with triphosgene standards prepared in diethylphthalate, with an initial decrement in colorimetric response, followed by a gradual increase, eventually reaching about 140% of the expected value after about 1 week of storage. In contrast, the triphosgene standards prepared in hexane solutions show no statistically significant bias in comparison to authentic gaseous phosgene standards. Thus all work using the colorimetric reference technique utilized triphosgene standards prepared from hexane stock solution. The hexane stock solution was sufficiently concentrated such that the small amounts added to the absorbing solution of 4-(4'-nitrobenzyl)-pyridine and N-phenylbenzylamine in diethylphthalate had no measurable effect on its background absorbance at 475 nm.

Liquid Chromatographic Determination of Phosgene-PYP Urea

Figure 2 illustrates a representative chromatogram of a sample containing phosgene-PYP-urea as well as the PYP derivatives of 2,4- and 2,6-

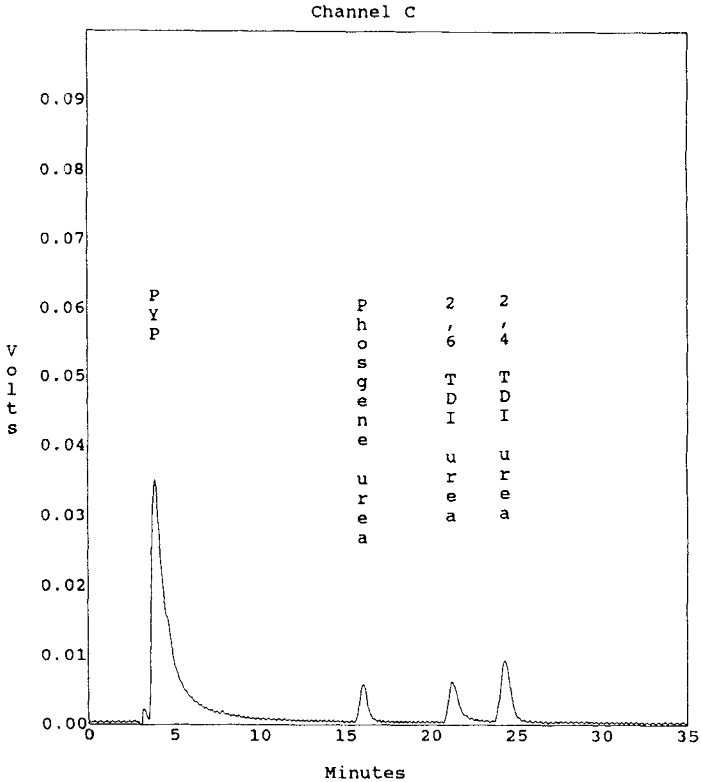


FIGURE 2 Chromatogram of sample containing phosgene-, 2,4-TDI-, and 2,6-TDI- PYP urea derivatives. Conditions: 30% acetonitrile / 70% aqueous ammonium acetate buffer, pH 6.0, isocratic at 1.5 mL per min. Supelcosil LC-18 DB column, 25 cm x 5 mm. (Channel C: UV absorbance at 254 nm; Channel D: UV absorbance at 270 nm).

toluenediisocyanate (TDI). In order to separate these compounds chromatographically, a slight modification of the mobile phase used for routine analysis was necessary. Thus a mixture of 30% acetonitrile and 70% buffer was used. Baseline separation of the three urea derivatives from the major peak of PYP was obtained in approximately 25 minutes, the retention time of the phosgene-PYP-urea being approximately 16 minutes under the

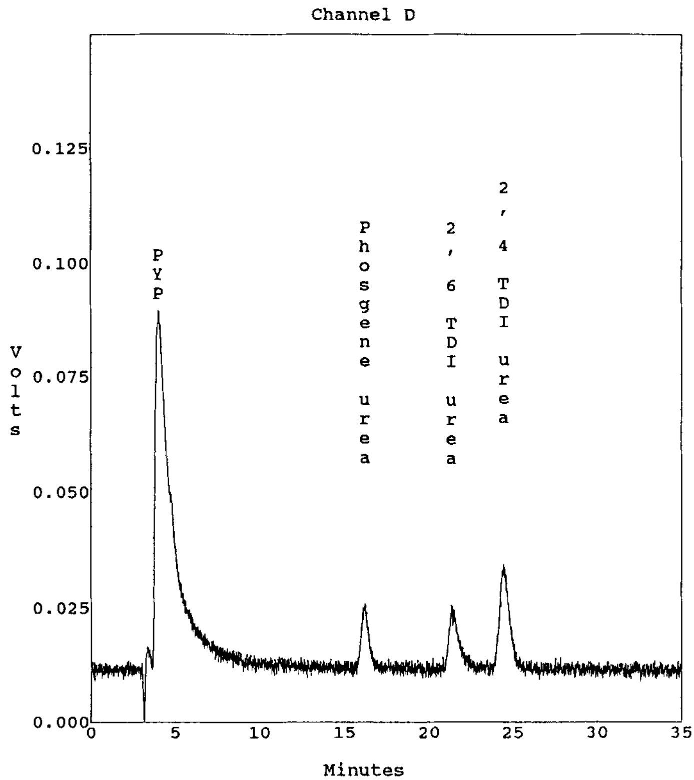


FIGURE 2 (continued)

chromatographic conditions. For analysis of samples suspected to contain only the phosgene urea, a mixture of 45% acetonitrile and 55% ammonium acetate buffer may be used. This results in more rapid chromatography, with the urea eluting at about 8.6 minutes.

Urea derivative prepared from phosgene and from triphosgene appeared identical in chromatographic characteristics. Figure 3 shows typical standard curves prepared from phosgene- and triphosgene-derived urea derivative. No statistical difference in response was noted. While acceptable calibration curves were obtained at either 254 or 270 nm, the response was more

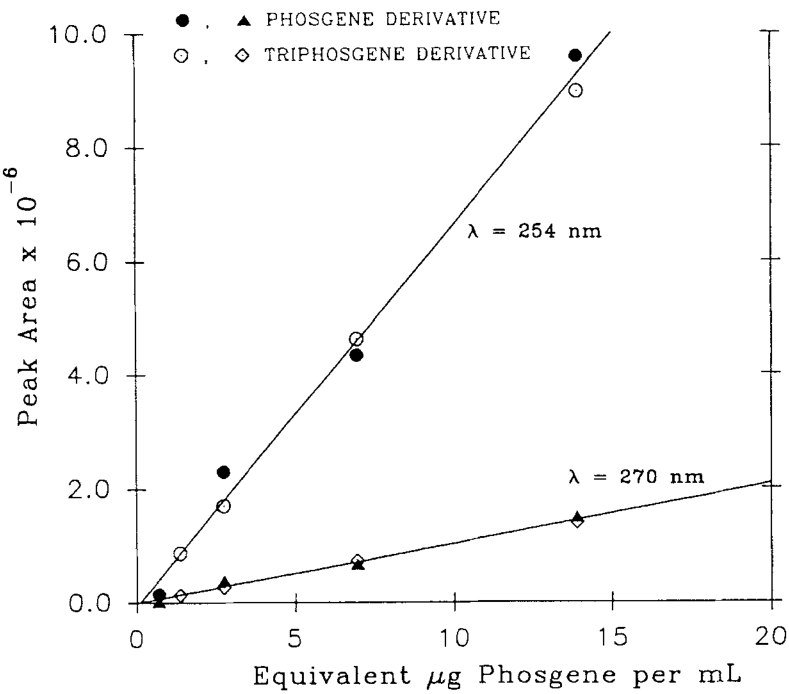


FIGURE 3 Calibration curves obtained from HPLC analysis of PYP-urea derivative prepared from phosgene and from triphosgene. Quantitation at 270 nm is recommended due to enhanced specificity and chromatographic stability. Estimated limit of detection at 270 nm is 0.4 μg phosgene per mL.

consistent at 270 nm, notwithstanding the greater sensitivity of analysis at 254 nm. In general the chromatograms exhibited a more stable baseline with fewer impurity peaks at 270 nm. Based on this, it is recommended that quantitation of urea derivative be accomplished using absorbance at 270 nm. The detection limit for measurement at 270 nm was approximately 0.4 μg phosgene per mL sample. This is equivalent to a 20 L air sample containing approximately 0.005 ppm phosgene, with desorption in 1 mL of acetonitrile.

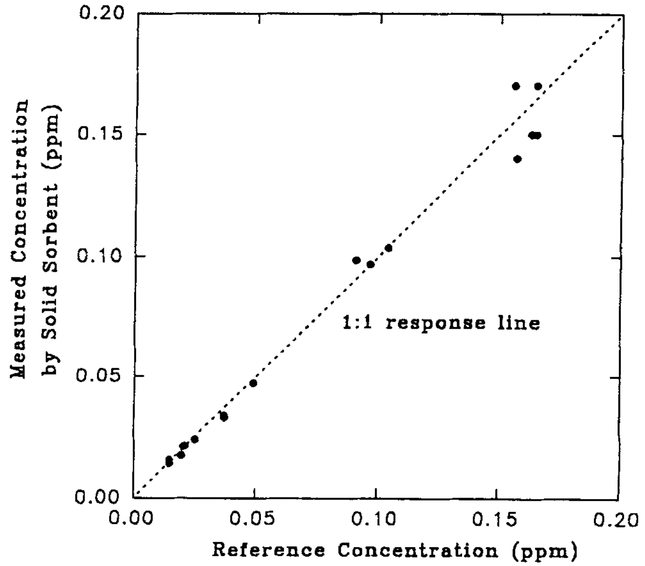


FIGURE 4 Performance of PYP coated solid sorbent for determination of phosgene at 25°C in dry air. Samples were collected at 1 L per min for 20 minutes, desorbed with acetonitrile and analyzed by HPLC. Reference phosgene concentration determined by gravimetric output of permeation tube or by colorimetric analysis.[4]

Performance of PYP Sorbent Tube

Test atmospheres of phosgene ranging from about 0.01 to 0.2 ppm (1/10 to 2 times the Occupational Safety and Health Administration's permissible exposure limit) were sampled with PYP sorbent tubes. This initial work utilized dry test atmospheres. Sorbent tube samples were collected at a rate of 1 L per min for 20 minutes. The test atmosphere concentration was determined from the gravimetric output of the phosgene permeation tube, and in addition, an impinger sample was usually collected for colorimetric analysis for verification. The results of analysis of the PYP sorbent tubes versus the expected test atmosphere concentration are shown in Figure 4. The recovery of phosgene from the samples was within ± 15% of the reference concentration over the entire range of phosgene concentrations. The average recovery was 96.9% (standard deviation = 6.85; range = 87.5 to 109%).

Test atmospheres of varying humidities were also sampled with PYP sorbent tubes. The target concentration of phosgene for these tests was 0.1 ppm, and the relative humidity ranged from 0 to 94% at 25°C. When compared to the phosgene concentration calculated from the gravimetric output of the permeation tube, both the PYP sorbent tube and the impinger / colorimetric techniques exhibited a strong effect of humidity on recovery of phosgene, as indicated in Figure 5. The apparent recovery of phosgene was nearly quantitative up to about 25% relative humidity and decreased to about 65% at 94% relative humidity. It is of interest to note that previous work has indicated that the colorimetric technique exhibits an apparent humidity effect, with losses of about 11% reported at 73% relative humidity.[7] In the present case, both the PYP and the colorimetric techniques were independently showing nearly identical humidity effects. Comparing the concentrations of phosgene determined by the PYP tube to the colorimetric technique, the average recovery of the PYP tube was 97.9 ± 2.1%. It is suggested that the observed humidity effect illustrated in Figure 5 was due to the true concentration of phosgene decreasing in the test atmosphere as humidity increases. Phosgene will undergo slow hydrolysis in the presence of moisture to yield hydrochloric acid and CO_2.[18] This type of hydrolysis has also been observed and studied in atmospheres containing isocyanate compounds,[19-20] and has been shown to be catalyzed by active surfaces, with the rate of hydrolysis occurring on surfaces being many orders of magnitude faster than that in the gas phase. Thus it is believed that both the PYP sorbent tube and the colorimetric technique were indicating the true concentration of phosgene in the test atmosphere, with the discrepancy between these techniques and the expected level of phosgene being due to hydrolytic decomposition of phosgene.

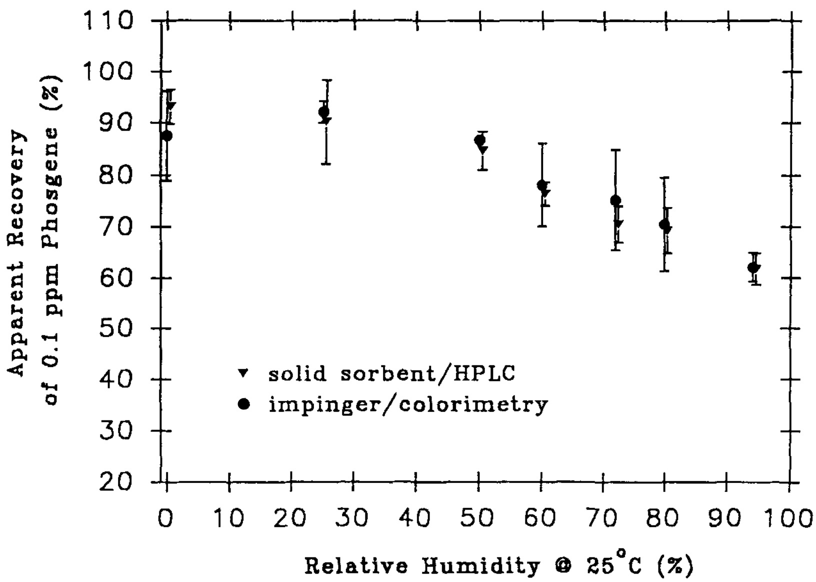


FIGURE 5 Comparison of PYP solid sorbent / HPLC and impinger / colorimetry for determination of phosgene in humid test atmospheres. Expected concentration of phosgene calculated from gravimetric output of permeation tube. Colorimetry and HPLC datapoints are slightly offset for clarity.

Sorbent tube samples collected from dry atmospheres containing 0.1 ppm of phosgene were evaluated for storage effects at varying storage temperatures and storage times. Three sets of samples were collected and then stored under one of the following regimens: one week at room temperature, one week at 4°C, or two weeks at 4°C. The percentage recoveries for these sets of samples are presented in Table I. Significant losses of phosgene were noted after a week of storage at room temperature and after two weeks at 4°C. However recovery was quantitative when sample tubes were analyzed within one week when stored at 4°C. In all cases, loss of phosgene derivative corresponded to the presence of a secondary peak appearing in chromatograms, indicating decomposition of phosgene-PYP urea. A similar phenomenon was

TABLE I

Storage Stability of Phosgene Collected on PYP Solid Sorbent*

Storage Conditions	% Recovery (mean ± s.d.)
one week at room temperature	92.8 ± 0.9 (n = 3)
one week at 4°C	102.7 ± 2.5 (n = 3)
two weeks at 4°C	89.9 ± 6.9 (n = 6)

* 20-L air samples containing 0.1 ppm phosgene. Temperature = 25°C; Relative Humidity = 0 %.

also noted to be occurring in the urea derivative synthesized in the laboratory and stored as the solid material under refrigeration. In this case, the secondary unknown peak would begin to appear in chromatograms of standards after about 5 months of storage. Thus it is recommended that sorbent tube samples be stored under refrigeration and analyzed within a week of collection, and that standards synthesized in the laboratory be stored for no more than a few months before expiration. Likewise, stock solutions of standards should be prepared on a weekly basis or sooner if secondary peaks begin appearing during chromatographic analyses.

CONCLUSIONS

1-(2-Pyridyl)-piperazine, a commonly used derivatizing agent for isocyanates, has been successfully adapted to use in a solid sorbent tube for collection / derivatization of airborne phosgene. Determination of the phosgene-PYP-urea derivative by reversed phase liquid chromatography is a sensitive and specific technique and offers the ability to simultaneously determine phosgene and isocyanates in contaminated atmospheres. The detection limit of the method is estimated to be approximately 0.005 ppm for a 20 L air sample, equal to 5% of the current OSHA permissible exposure level of 0.1 ppm. While the performance of the PYP sorbent tube in the laboratory was satisfactory, further testing under field conditions is warranted in light of problems encountered under certain sample storage conditions.

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