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Development of a Quantitative, Sampling and Analytical Method for Acetone Cyanohydrin in Air

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Acetone Cyanohydrin

I. Abstract

The air sampling and analytical method for acetone cyanohydrin involved collection of the analyte on Porapak QS, a silylated styrene-divinylbenzene porous polymer. The samples were desorbed with ethyl acetate and an aliquot of this solution was analyzed by gas chromatography using a nitrogen-phosphorous detector and a teflon column packed with 5% OV-17 on Chromosorb T. The detection limit was estimated to be 0.1 µg/mL acetone cyanohydrin in ethyl acetate. The method was tested over the range 1.0-50 µg/sample. Quantitative recovery was obtained for samples stored for one day at ambient temperature or for periods up to seven days if the samples were refrigerated.

II. Introduction

Acetone Cyanohydrin (2-hydroxyisobutyronitrile) is produced by the reaction of acetone with hydrogen cyanide in the presence of base (1). The compound is highly reactive. It is readily hydrolyzed by water to form acetone and hydrogen cyanide; however, this reaction occurs very slowly when the pH is reduced to 1-2 (2). It undergoes reaction with nucleophiles such as amines to yield α-aminonitriles (3). The material is also thermally unstable probably dehydrating to form methacrylonitrile (2). Acetone cyanohydrin has been used widely in the plastics industry for the production of methacrylate resins (see Figure 1)(4). Although another process has been developed to produce these polymers, the extent of its usage is unknown (5).

The principal route of exposure to acetone cyanohydrin is dermal; however inhalation may also be an important route. Its toxicity is directly related to its ability to readily dissociate and release hydrogen cyanide (HCN) and acetone. In the body this release of HCN produces a cyanotic condition where cyanide ion competes with oxygen for binding sites on hemoglobin. An LD_{50} of 120 mg/kg has been reported for guinea pigs exposed dermally to acetone cyanohydrin. Due to the acute toxicity of the material (estimated to be 18 times as toxic as acetonitrile via inhalation), NIOSH has recommended a ceiling concentration limit of 1 ppm (3.5 mg/m^3) for any 15-minute exposure period (6).

Due to the widespread usage and toxicity of acetone cyanohydrin, a method was needed to monitor worker exposure. A literature search turned up several reported analytical methods for acetone cyanohydrin. Among these were colorimetric techniques (7, 8, 9), amperometry (10), chemiluminescence (11) and gas chromatogaphy (12). However, all of these methods required that the analyte be collected in an impinger or that the analysis be completed after collection of a sample, or were specific only for cyanide ion. In addition none of the references provided adequate information concerning the accuracy and precision of the developed methods.

Method development was initiated using the following considerations. Sampling would be accomplished by collecting the analyte on a sorbent, such as a porous polymer, which has minimal capacity for water vapor. Analysis would be accomplished by gas chromatography using those conditions necessary to minimize thermal degradation and adsorption of the analyte on the column.

The following criteria were employed for validation of the method:

A. Recovery from the sampling medium should be at least 80%.

B. The relative standard deviation (RSD) of the overall sampling and analysis procedure should be no greater than 10.0%.

C The bias of the method from an independent method should be no more than 15%.

D. The mean of the results obtained with samples analyzed immediately after collection should not differ statistically at the 95% confidence level from the means of results obtained with samples analyzed after storage for 7 days.

One specific task of the method development was to find the lowest level of the analyte that could be recovered from the sampling medium with at least 80% desorption efficiency and with a relative standard deviation of 10%. This is referred to as the least analytically quantifiable level (LAQL).

The purpose of this report is to present the major points of the research effort that went into the development of the sampling and analytical method for acetone cyanohydrin. The analytical procedure that was developed is included as Appendix A to this report.

III. Analytical Method Development

The thermal instability of acetone cyanohydrin presented a significant challenge to development of a gas chromatographic method. A Perkin-Elmer Model Sigma-2 gas chromatograph equipped with a flame-ionization detector was used in the initial phases of the development work. Several gas chromatographic packings including Tenax G.C., 3% Dexsil on Chromosorb W AW, 10% SP 1200 + 1% H_3PO_4 on Chromosorb W AW, 10% DEGS + 1% H_3PO_4 on Chromosorb W AW, 10% SP 210 on Supelcoport, 10% TCP on Chromosorb P AW, and 10% DEGS + 1.0% H_3PO_4 on Chromsosorb T were loaded into glass columns (1-2 m). Replicate injections of 5 µL of the analyte in CS_2 (1-10 µg/µL) were used to evaluate the precision of analysis. Temperatures of the columns ranged from 30 °C to 120 °C. The injector and detector ports were maintained at 75 to 150 °C In all cases peak areas were non-reproducible and peak shapes exhibited significant tailing characteristic of thermal degradation of the analyte. This problem

was so severe that it was decided to evaluate a Teflon column using Chromosorb T (40/60 mesh) as the support for a variety of liquid phases. These coatings were 5% OV-17, 5% OV-17 + 0.5% H_3PO_4 and 10% DEGS + 0.5% H_3PO_4. The packing materials were prepared according to the evaporative coating techniques described in Reference (13). They were refrigerated (per instructions in reference 13) prior to packing into 2 m X 4 mm i.d. Teflon columns. A plug of silanized glass wool was pushed 7 in. into the front (injector) end of the column. The packing material was then added from the other end. The septum fitting as well as the stainless steel injection port insert and quartz liner were removed from the Sigma-2 chromatograph and the unpacked end of the column pushed in from the oven side of the G.C. to where it extended past the outer injection port threads. It was then trimmed even with the injection port and the septum fitting replaced. Nylon Swagelok (1/8") fittings and ferrules were used to connect the column to the injector and detector port end fittings.

The selection of a desorbing solvent was based on the following rationale. The use of carbon disulfide as a desorbing solvent is generally precluded, when porous polymers are used as sorbents, since it dissolves many of them. This leads to problems such as fouling of syringes with gums, etc. It was necessary to eliminate hygroscopic solvents such as acetone from consideration due to possible degradation of the analyte by moisture. Ethyl acetate was selected. It is relatively non-hygroscopic and is compatible with porous polymers and nitrogen-phosphorous detectors. The analyte was quite soluble in this solvent.

All of the columns were evaluated initially with a flame-ionization detector under the following nominal conditions:

H_2 flow	(60 mL/min)
Air flow	(450 mL/min)
Carrier (N_2)flow	(25 mL/min)

The temperatures of the injector and detector ports and the column were maintained at 100 °C and 70 °C, respectively. Five-microliter aliquots of the analyte (100 µg/mL) were injected onto the column. Generally, reproducibility was good after the column had been passivated with several injections of concentrated analyte in CS_2. Retention times for the analyte varied from 3.2 min (5% OV-17) to 9 min (5% OV-17 + 0.5% H_3PO_4) to 31 min (10% DEGS + 1% H_3PO_4). Further work with DEGS was abandoned because the retention time of the analyte was so long and the peak shape too broad to realistically quantitate under the above operating conditions.

During the course of this initial evaluation it was found that deposits of brown-polymeric material built up in the glass-lined transfer line to the detector. Apparently, this was the "reactive zone" in the column that required passivation. This transfer line was removed from the gas chromato-

graph, a small plug of 1/8 in. o.d., 1/16 in. i.d. Teflon tubing pushed into the detector end of the column and a 3 in. length of 1/16 in. o.d. Teflon tubing pushed into the center of the plug. The nylon ferrule and compression fittings on the detector end of the column were pushed over the plug and tightened down in this position when the column was reconnected to the detector. The arrangement allowed the column to be butted up very close to the detector base. This then gave a system where the analyte came into contact only with Teflon or the packing material. The modified column design is shown in Figure 2.

The two remaining columns were evaluated using a nitrogen-phosphorous detector (NPD). The air and hydrogen flows were changed to 175 mL/min and 5 mL/min. All other conditions remained the same. Five-microliter aliquots of a solution containing 10 µg/mL acetone cyanohydrin in ethyl acetate were injected onto the column. Reproducibility of replicate injections was good (~3%) for both columns. With prolonged usage, retention times of the analyte on the H_3PO_4-treated column changed drastically. In addition, bleed from this column produced adverse effects upon the rubidium bead of the detector. Intermittent noise spikes and rapid loss of sensitivity of the bead were observed. Therefore, it was decided to proceed with the 5% OV-17 column.

Further problems with rapid fatigue and deterioration of NPD beads on the Sigma 2 gas chromatograph necessitated that a switch to a Varian 3700 GC be made. The only modification made to the column was that the unpacked (injector) end was trimmed back to fit in a shorter Varian on-column injection port. This therefore left a 7.5-cm flash-vaporization zone in the injection port end of the column.

The precision of replicate determinations for 5-µL aliquots injected onto the OV-17 column over the range 0.1-50 µg/mL of acetone cyanohydrin in ethyl acetate is shown in Table 1. The detection limit (RSD of replicate injections 10%) was estimated to be 0.1 µg/mL. Calibration curves over the range 0.5-5.0 µg/mL and 5.0-50 µg/mL are shown in Figures (3a) and (4b). A study was made to compare the linearity of detector response using peak heights versus peak areas. Over the range 0.5 - 100 µg/mL, the correlation coefficients (r) using either technique were comparable. In the concentration range 100-1000 µg/sample, however, the peak-height response gave a less satisfactory linear correlation coefficient ($r = 0.956$) than did peak area ($r = 0.991$). This may have indicated that the detector was being saturated. Alternatively it may have indicated column overload.

A chromatogram showing the elution of the analyte on the 5% OV-17 column is shown in Figure (4a). Although this type of column displays inherently poor resolution, it does allow the analyte to be readily identified and quantitated in the presence of co-contaminants if the NPD is used as a detector. A chromatogram of a solution containing 100 µg/mL each of acetone cyanohydrin and three possible co-contaminants - acetone, methyl alcohol and

methyl methacrylate, all in ethyl acetate - is shown in Figure (4b). The chromatograms in Figures (4a) and (b) appear to be identical and the area of the analyte peak is the same regardless of whether it is found alone or in the mixture. Another potential co-contaminant - acrylamide - could not be eluted from the column.

IV. Collection Medium Development

Two types of tests were used to evaluate sorbents - stability and capacity tests. In addition, the stability of the analyte on the materials used to contain the sorbents in collection tubes was evaluated.

A. Stability tests.

1. Stability of analyte on sorbent. A variety of porous polymers were evaluated for storage of the analyte. All were cleaned according to the following procedures

   - extraction in a Sohxlet apparatus with 80/20 v/v acetone/methanol for 4 hours
   - Sohxlet extraction with hexane for 2 hours
   - drying by purging with N_2 for 2 hours at 120 °C with the device shown in Figure 5.

   One- and seven-day storage samples were prepared by metering 2.8 µL aliquots of a solution containing 10 µg/µL of the cyanohydrin in ethyl acetate onto 100-mg beds of the porous polymers, which were contained in crimp-cap sample vials. Two samples using each sorbent were prepared. After storage at room temperature in the dark for the indicated period they were desorbed in 1.0 mL of ethyl acetate and analyzed by GC-NPD. The results are presented in Table (2).

   Although the analyte was shown to be stable on several sorbents, Porapak P was chosen for initial evaluation. This is a non-polar styrene-divinylbenzene co-polymer, which has a relatively large surface area - 306 m^2/g (15). It was thought that the low polarity of the sorbent would minimize its capacity for reactive co-contaminants such as water vapor. Follow-up tests to study the storability of 0.5-5.0 µg of the analyte on 100-mg beds of this polymer indicated a stability problem. At the 0.5-µg/sample level, only 41% (RSD = 42%) recovery was obtained after 7 days storage at room temperature. Therefore, it was decided to evaluate 60/80 mesh Porapak QS, a relatively nonpolar styrene-divinylbenzene copolymer, which has been treated with a silylating agent to eliminate any reactive sites on the polymer. The surface area of this material is 634 m_2/gm (14). The stability of 0.5-50 µg of

acetone cyanohydrin on 100-mg beds of Porapak QS was evaluated after storage for 1 or 7 days at room temperature. The results of this study are presented in Table (3). Recovery was quantitative for all levels regardless of the storage period. However, there was a statistically significant difference (at the 95% confidence level) between the 1 and 7 day storage samples at the 5-µg/sample level.

Although 100-ng/mL standards of the analyte in ethyl acetate could be analyzed with a precision of 6.2%, recovery studies at these lower levels were not performed. The method will allow samples to be taken from atmospheres containing about one-tenth the recommended threshold limit value (TLV) amounts of acetone cyanohydrin (15 min X 0.35 µg/L X 0.1 L/min = 500-ng). Therefore 500-ng was defined as the LAQL.

2. Evaluation of Sorbent Retaining Material. During the course of this study, it was found that 1- or 10- µg samples collected onto 100-mg beds of Porapak QS from U-tubes and exposed to humid air from a bubbler containing a saturated KCl solution (80% RH) for 15 minutes could not be stored for periods up to 4 days at room temperature. Recoveries averaged 75-80% of the amounts spiked onto the tube. This was despite the fact that breakthrough had not occurred and for samples stored 1 day recovery was quantitative (90%). The front glass-wool retaining plugs were desorbed separately in 1.0 mL of ethyl acetate. It was found that a significant amount of the analyte (3-4%) was being collected on these plugs. This silanized glass wool had a foul (amine-like) odor, indicating it might have become contaminated with an amine that was degrading the cyanohydrin. Therefore, the glass wool was cleaned by refluxing with acetone (distilled in glass) in a Sohxlet extractor for several hours and then dried in a vacuum oven. In order to determine whether decomposition was occurring on the sorbent or the glass wool, two tubes were prepared by using small plugs of the glass wool to hold 100-mg front and 50-mg backup sections of the sorbent in place. Four additional tubes were prepared using Teflon wool that had been similarly extracted and dried as described above. Two of these tubes were packed using Teflon wool to contain both sections of sorbent. The front sections of Teflon wool were not packed into the two other tubes so that the analyte would be collected only on the sorbent.

One and ten-microgram per tube samples were then collected from U-tubes and exposed to humid air as described above. The samples were analyzed after storage for 4 days at room temperature in the dark. The results are shown in Table (4). With the exception of collection tube #6 the percent recovery was very similar in all of the samples (70-80%). It was concluded that the type of packing material used was probably irrelevant since decomposition is

apparently being caused by trace amounts of water vapor co-adsorbed with the analyte on Porapak QS. In addition, the current commercial nonavailability of Teflon wool would preclude its practical usage.

B. Capacity Tests

Since it was not possible to accurately monitor the concentration of dynamic atmospheres of acetone cyanohydrin in humid air (see section 8), capacity tests were performed as follows. A U-tube was connected at one end to a bubbler containing a saturated solution of potassium chloride in water and on the other end to a sorbent tube containing 100-mg front and 50-mg back up sections of Porapak QS, held in place with silanized glass wool plugs. The back end of the sorbent tube was connected to a pump. The pump was started and aliquots of solutions of acetone cyanohydrin in ethyl acetate ranging from 10-100 µg/µL per injection were spiked into the U-tube. The analyte was collected in the presence of the water vapor at 0.2 L/min for 60 min. The samples were then analyzed by gas chromatography after desorbing in 1.0 mL of ethyl acetate. The front silanized glass-wool plug was combined with the front sorbent section and the separating plug of glass wool with the back up section. The results are presented in Table (5). The percent breakthrough appeared to remain constant throughout the loading range evaluated and never exceeded 2%. It is likely that this type of experiment represents a worst possible case situation for testing the capacity of the sorbent. This is due to the fact that the sorbent was challenged with:

- a very high concentration of the analyte during the first few minutes of the capacity tests, (It appeared that the cyanohydrin had completely evaporated during this period.)
- a large amount of ethyl acetate (5-25 mg), and
- a large amount of water vapor (221 mg at 80% RH).

In any case it is possible that the sampling device would have had a greater capacity for the analyte had it been possible to eliminate the first two of the above situations.

C. Recommended sampling device.

It is recommended that the sampling device consist of a 100-mg front and 50-mg backup section of Porapak QS. These sections should be held in place by small plugs of silanized glass wool. It may be necessary to extract the glass wool with acetone prior to usage. The tube has the capacity to collect at least 9.5 times the NIOSH recommended exposure concentration of 3.5 µg/L for a 15 minute period. Although the analyte was unstable if collected from a humid atmosphere and stored at room

temperature, storage at 0 °C for 5-7 days gave recoveries of 92.2%, 102.8% and 98.1% for the sorbent spiked at the 1-, 10-, and 50-µg/sample level. The mean pressure drop across 5 sorbent tubes was found to be 15.4 in. of H_2O (RSD = 7.1%) at a flow of 0.19 mL/min. Although this pressure drop is large, it should not present an overwhelming problem to sampling, since the collection period is only 15 minutes. Longer term sampling should be done at lower flow rates.

V. Evaluation of the Total Method

This method was evaluated by collecting 1 to 50 µg of the analyte using the previously described sorbent tubes at a temperature of 22 °C and a pressure of 740 torr. The samples were collected from U-tubes that had been connected to the collection tube with Nylon Swagelok fittings. Ethyl acetate solutions of acetone cyanohydrin were injected (1.0, 10.0 and 50 µg in 5, 10, or 25 µL of solvent) into the U-tube and the analyte was evaporated onto the sorbent by pulling air through the sampling train for 1.0 hour at nominal flow rates of 0.2 L/min. The open ends of the U-tubes were then connected to bubblers containing saturated KCL solutions and the sorbent tubes exposed to humid air (RH = ~80%) for an additional 15 minutes. The tubes were then stored from 1 to 7 days prior to analysis. The long-term storage samples were capped and refrigerated at 0 °C. In addition they were placed in a capped graduate cylinder to preclude further problems with moisture or vaporized contaminants that were present in the refrigerator.

In the analysis, the front sorbing section was combined with the front glass-wool plug and the backup section with the separating glass-wool plug. The results from both storage studies are shown in Table 5. Breakthrough to the backup section did occur in some of the 50-µg samples. The maximum weight percent of total sample which broke through to the backup section was 2%. Quantitative recovery was obtained after storage of the samples at 0 °C throughout the analytical range. The recovery of the long-term storage samples did not differ statistically at the 95% confidence level from the 1-day storage samples. The results have not been corrected for desorption efficiency.

VI. Conclusions and Summary of Statistical Results

The results were analyzed using statistical procedures described in Reference (16). The pooled relative standard deviation (RSD_T) of the method was calculated using the following individual contributions:

RSD_1 = 4.2% (one-day storage samples only - see Table 3. This data passed Bartlett's criterion for homogeneity of variance.)

RSD_2 = 8.9% (one day storage samples only - see Table 7. This data passed Bartlett's criterion for homogeneity of variance.)

The variation in the pump flow (RSD_p) was assumed to be ± 5%. No correction for imprecision due to variation in desorption efficiencies was applied to the calculation of the overall precision The pooled relative standard deviation was calculated to be 9.3% which is within the established limits of the protocol.

It was not possible to fulfill requirement C of the protocol, since analyte-in-air concentrations could not be monitored accurately. Although the statistical criteria for sample storage (D of the protocol) were met, this was achieved only by refrigerating long-term storage samples immediately after collection. This may not adversely restrict the use of this method, since portable refrigerants, such as Koolit (FDC Pkg. Inc. Medford, Mass.), are available in which to pack the samples. Finally, the LAQL was established at a higher level than was dictated by the precision and accuracy requirements. The method will still enable the determination of one-tenth the recommended TLV concentrations of acetone cyanohydrin in air.

VII. Dynamic Generation System.

Figure 6 shows the generation system. Test atmospheres of cyanohydrin in humid air (relative humidity = 80%) were generated dynamically by passing clean dry air from Line A at 10-20 cm^3/min through a fritted bubbler (D) containing liquid acetone cyanohydrin maintained at 42 °C in a constant temperature bath (C). The vapor then was carried to mixing chambers (J.K.), where dilution air from Line B was added at 3000 cm^3/min, and finally to a seven-port sampling manifold (L), which was vented to an exhaust hood. The dilution air was humidified by passing it over water in two containers (E,F) that were placed serially in line immediately before the mixing chamber. The flowrates of the contaminant stream and dilution air were monitored with mass flowmeters (G,H)(Hastings Raydist Co. Hampton Va). The temperature and relative humidity of the dilution air were monitored with an electronic hygrosensor (I)(Humitemp, Phys-Chem Research Corp. New York, N. Y.) placed downstream of the water containers. All components of the generation system were constructed of glass or polyfluoroethylene.

VIII. Independent Methods Evaluated for the Determination of Acetone Cyanohydrin in Air.

Although it was possible to dynamically generate acetone cyanohydrin in humid air, it was not possible to independently verify the concentration of the analyte. The problems with each technique evaluated are detailed below.

A. Continuous Monitors

1. Total hydrocarbon analyzer. Bag standards, prepared by injecting neat acetone cyanohydrin (100-1000 µg) into 30 L of dry air could

not be used to calibrate the total hydrocarbon analyzer (Bendix Model 8401, Bendix Instruments, Beckley, W. Va., 26003) which was being evaluated as a continuous monitor. The response did not level off; rather, it continued to rise as the bag was evacuated into the analyzer's sampling port. In addition, the chromatographic response would periodically increase rapidly and decrease by tailing, possibly due to thermal degradation of the analyte in the transfer lines.

2. Photoionization detector. This detector was noisy and not very sensitive even for concentrations of analyte in dry air as high as 33 µg/L. The detector response also increased as the bag was evacuated. In addition, the detector was much more sensitive to other contaminants, such as acetone, which were drawn into the hood where the detector was being evaluated.

B. Impinger Techniques

1. Collection of the Analyte in Solvents. A variety of solvents, including carbon disulfide, hexane, cellosolve acetate and n-decane were evaluated as trapping media in impingers being used to collect acetone cyanohydrin. Each solvent was evaluated by simultaneously collecting samples of the analyte from bag standards on the Porapak QS sorbent tube and in impingers (front and backup containing the solvents). These impingers were maintained at -10 °C by immersion in a Dewar flask containing an ice-salt bath. The only solvent which had an adequate capacity for the analyte was n-decane. The amounts recovered from the impinger agreed well with those obtained with the sorbent tubes for concentrations ranging from 0.33 µg/L to 33.3 µg/L when synthetic standards prepared in Tedlar bags were used. Recovery (relative to the bag standard concentration) was 80% over this range. However the analysis of samples taken by impinger and sorbent tube from the dynamic generation system at an approximate concentration of 10 µg/L and a relative humidity of ~80% indicated poor agreement between the two techniques. Generally, the impingers gave results that were lower than those obtained from the sorbent tube. It was observed that water vapor was condensing inside the impinger and apparently decomposing the analyte.

2. Ion-specific Electrode. The contaminant stream was collected in impingers containing 0.1M Sodium Hydroxide (NaOH) and converted to cyanide. A cyanide ion specific electrode was then used to determine the concentration of analyte in the impinger. Trial runs with known quantities of analyte evaporated from U-tubes at 0.2 L/min

into the impinger gave results that were 118% of the controls (prepared by injecting the same quantity of analyte into the same volume of NaOH solution as was in the impinger). Several problems were apparent when using this technique however, including sluggish response from the electrode and pronounced degradation (pitting) of the electrode with time. In addition, the analysis of samples obtained in the impingers from the generation system and analyzed via the ion-specific electrode indicated that six times the amount of cyanohydrin was being trapped in the impingers as was being collected on the sorbent tubes. The analyte was apparently being decomposed by water vapor in the generation system. The HCN so produced was trapped in the impinger, but not in the sorbent tube (although it would not have affected the analysis whether it had been trapped or not, since it was readily separated from the analyte by the analytical method).

C. Sorbent Sampling

1. Derivatization Approach. An attempt was made to convert the cyanohydrin to a trimethylsilyl derivative for analysis via GC-FID. This was to be accomplished by collecting the analyte on Porapak QS, derivatizing it directly via desorption with trimethylchlorosilane (TMCS), and analyzing the derivative on a 5% OV-210 on Gas Chrom Q column with a programmed run from 50-120 °C. Although the 100-µg amounts of the cyanohydrin could be readily derivatized after 0.5 hr contact with the TMCS, it was not possible to quantitatively recover 100-µg quantities of the analyte from Porapak QS. The retention time of the derivative on the column changed drastically after prolonged repetitive injections. In addition, the derivative appeared to be sorbed by the column. This was evidenced by a periodic disappearance of derivative peak from one analysis to the next.

2. Direct Recovery from Porapak QS. An attempt was made to recover the analyte directly from the Porapak QS with CS_2 as a desorbing solvent and analysis by GC-FID using a teflon column (5% OV-17 + 0.5% H_3PO_4 on Chromosorb T). Recovery was 90% for samples of the analyte below 100-µg per 100-mg bed of sorbent, using 1.0 mL of CS as the desorbing solvent. There was good (100%) agreement between results from the two methods for samples collected from the generation system at 70 µg/L. However, subsequent tests showed that the independent technique yielded lower recoveries than the analytical technqiue. Further work on this method was abandoned due to time restrictions.

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Table 1

Precision of Gas Chromatographic Analysis of Standard Solutions of Acetone Cyanohydrin in Ethyl Acetate Using 5-µL Injections

Level (µg/mL)	Number of Replicate Injections	RSD,%
50	3	2.0
5	3	2.0
0.5	6	4.0
0.1	5	6.0

Table 2

Results of Screening Tests for Storability
of Acetone Cyanohydrin on Various Porous Polymers[a]

Sorbent	Mesh Size	Percent Recovery (%) 1-Day Storage	7-Day Storage[b]
Chromosorb 101	60/80	115	103
Chromosorb 102	"	71	0
Chromosorb 103	"	0	0
Chromosorb 104	"	108	67
Chromosorb 105	"	105	98
Chromosorb 106	"	98	65
Chromosorb 107	"	111	61
Chromosorb 108	"	95	34
Porapak N	50/80	100	98
Porapak P	"	100	100
Porapak Q	"	103	90
Porapak QS	"	106	100
Porapak R	"	100	97
Porapak S	"	82	30
Porapak T	"	98	97

a. 100 mg of each sorbent spiked with 28 µg of acetone cyanohydrin

b. Storage at ambient temperature in the dark

Table 3

Recovery of Acetone Cyanohydrin from Porapak QS over the Range 0.5–50 µg/Sample After Storage for One and Seven Days

Loading Level (µg)	Percent Recovery	
	1-Day Storage	7-Day Storage
50	97	101
	98	99
	101	96
	100	100
	101	98
	102	96
Mean	100	2.1
RSD, %	1.9	
$t_{calculated}$[a]		1.7298
5	102	100
	104	97
	104	99
	102	98
	101	96
	97	95
Mean	102	98
RSD,%	2.5	1.9
$t_{calculated}$[a]		3.1203
0.5	108	97
	108	
	101	106
	95	98
	95	101
	94	97
Mean	100	100
RSD,%	6.5	3.5
$t_{calculated}$[b]		0
RSD_1,%[c] = 4.2		

a. $t_{0.95}$, 10 degrees of freedom = 2.228 (15)

b. $t_{0.95}$, 9 degrees of freedom = 2.262 (15)

c. pooled relative standard deviation

Table 4

Evaluation of Stability of Acetone Cyanohydrin on Sorbent Retaining Materials and on Porapak QS after Exposure of Vapor-Spiked Samples to Humid Air[a]

Collection Tube	Packing Materials[b,c]	Loading Level(μg)	Percent Recovery(%) Front Plug	Sorbent	Total
1	Teflon FCB	10	4	69	73
2	" "	1	N.D.	75	75
3	" CB	10	-	77	77
4	" "	1	-	81	81
5	Glass Wool FCB[d]	10	8	69	77
6	" " FCB	1	N.D.	62	62

a. All samples were collected from U-tubes for 1.0 hr. and exposed to humid air for 15 min. They were stored at ambient temperature for 4 days in the dark.

b. F = Front, C = center, B = Back.

c. extracted with acetone

d. silanized

N.D. not determined

Table 5

Breakthrough Studies[a]

Loading Level	% Recovery		
	Front	Back	Total
10 µg	101	2	103
25 µg	96	1	97
50 µg	90	1	91
100 µg	92	1	92

a. Samples were prepared by loading U-tubes with 5-25-µl aliquots of ethyl acetate solutions containing 10, 25, 50, or 100 µg of acetone cyanohydrin. The aliquots were evaporated onto the sorbent tubes by pulling humdified air (80% relative humidity) through at 0.2 L/min. for 60 min.

Table 6

Data from Study of Stability of Acetone Cyanohydrin Collected from U-tubes on Porapak QS and Exposed to Humid Air (RH = 80%) for 15 Minutes

Loading Level µg	Storage Period(d)	% Recovery	Storage Period(d)	% Recovery
50	1	101.5	5	102.6
		80.0		94.3
		93.8		97.4
		90.0		94.9
		79.0		102.7
				96.6
	Mean	88.9	Mean	98.1
	RSD,%	10.6	RSD%	3.8
			t_{calc}[a]	1.8448
10	1	103.4	7	104.2
		98.7		102.7
		86.5		90.6
		100.6		107.4
		96.0		103.9
		87.8		107.9
	Mean	95.5	Mean	102.8
	RSD,%	7.2	RSD,%	6.1
			t_{calc}[b]	1.894
1	1	80.2	6	91.5
		94.5		93.9
		103.9		91.6
		99.2		92.1
		96.2		92.1
		100.5		
	Mean	95.8	Mean	92.2
	RSD,%	8.7	RSD,%	1.1
			t_{calc}[a]	1.00618

$RSD_2,\%$[c] = 8.9

a. $t_{0.95}$, 10 degrees of freedom = 2.228 (15)

b. $t_{0.95}$, 9 degrees of freedom = 2.262 (15)

c. pooled relative standard deviation

Index of Tables

Index of Figures

Figure 1. Major industrial uses of Acetone Cyanohydrin.

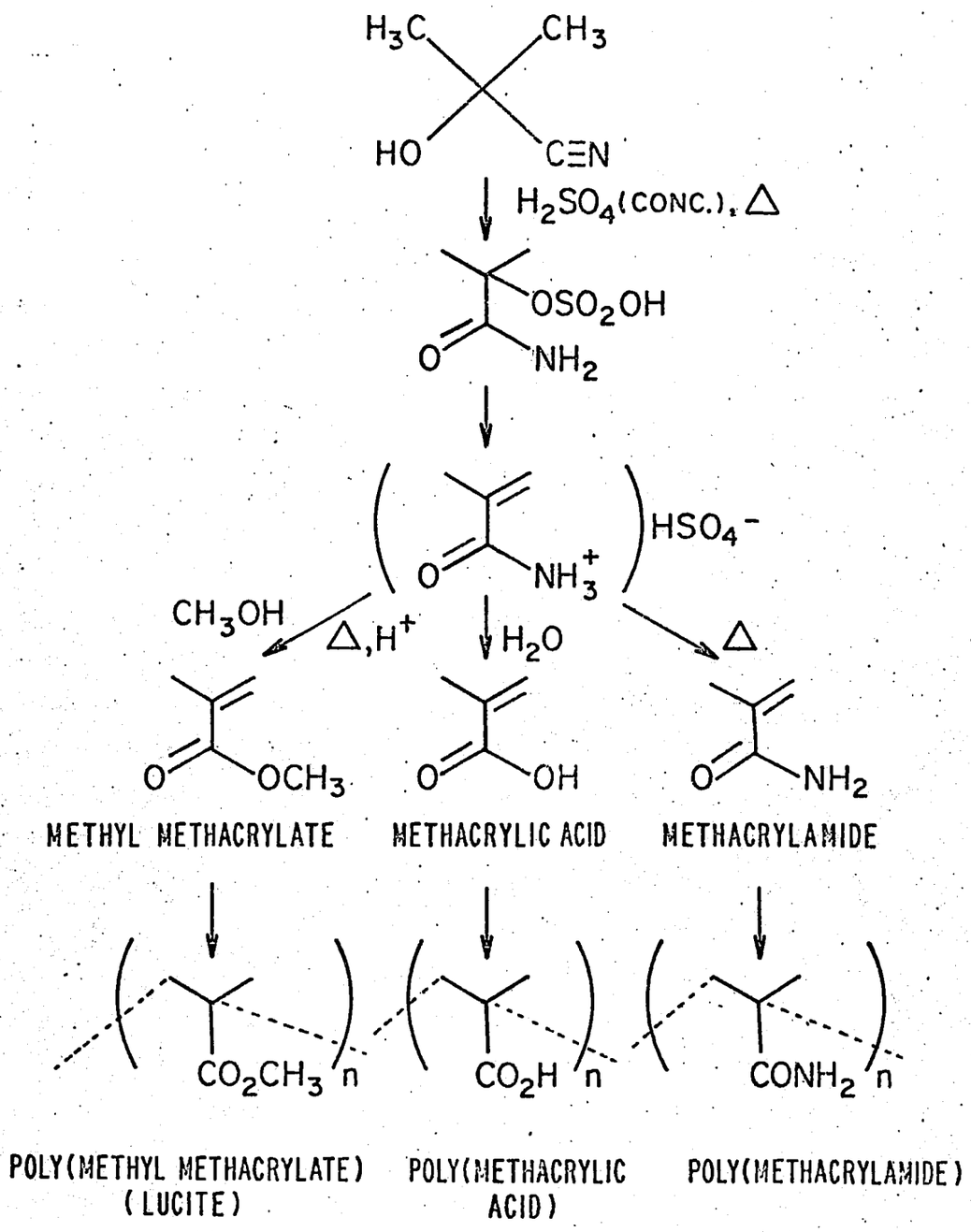
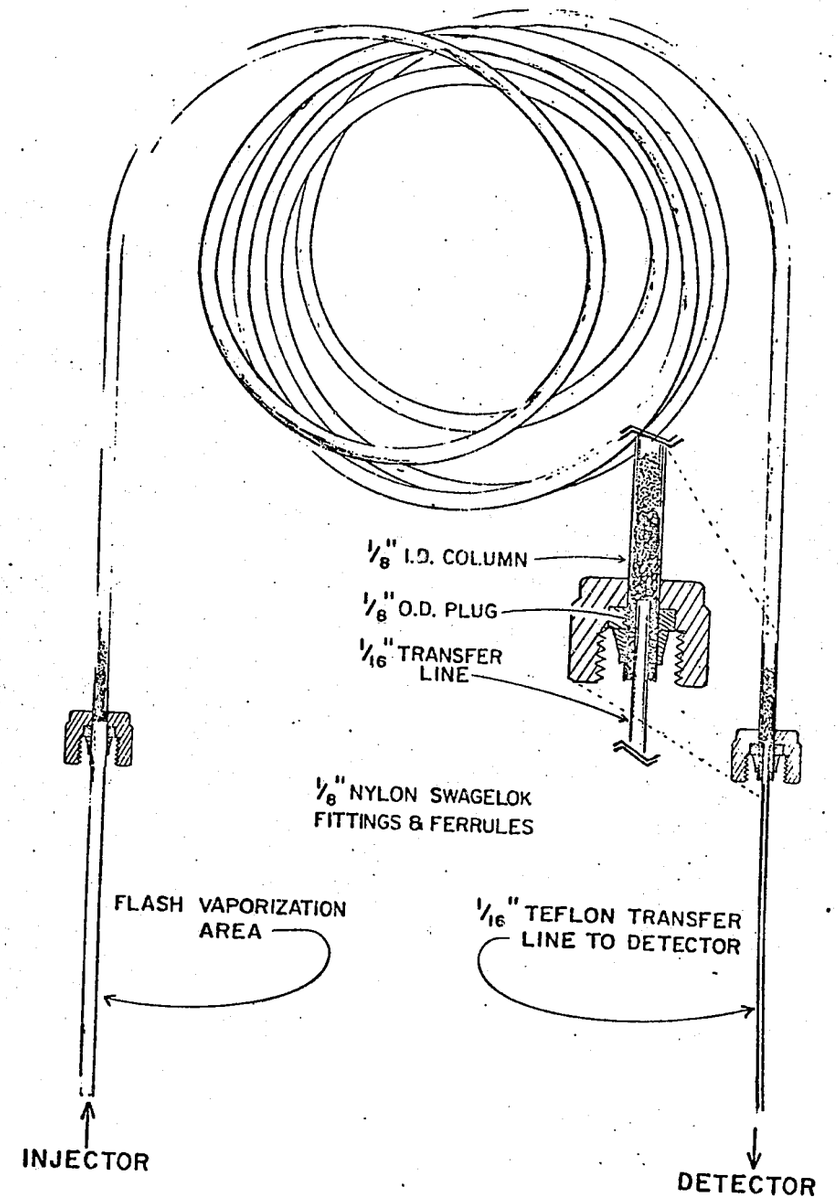


Figure 2. All Teflon gas chromatographic system used for the analysis of acetone cyanohydrin.



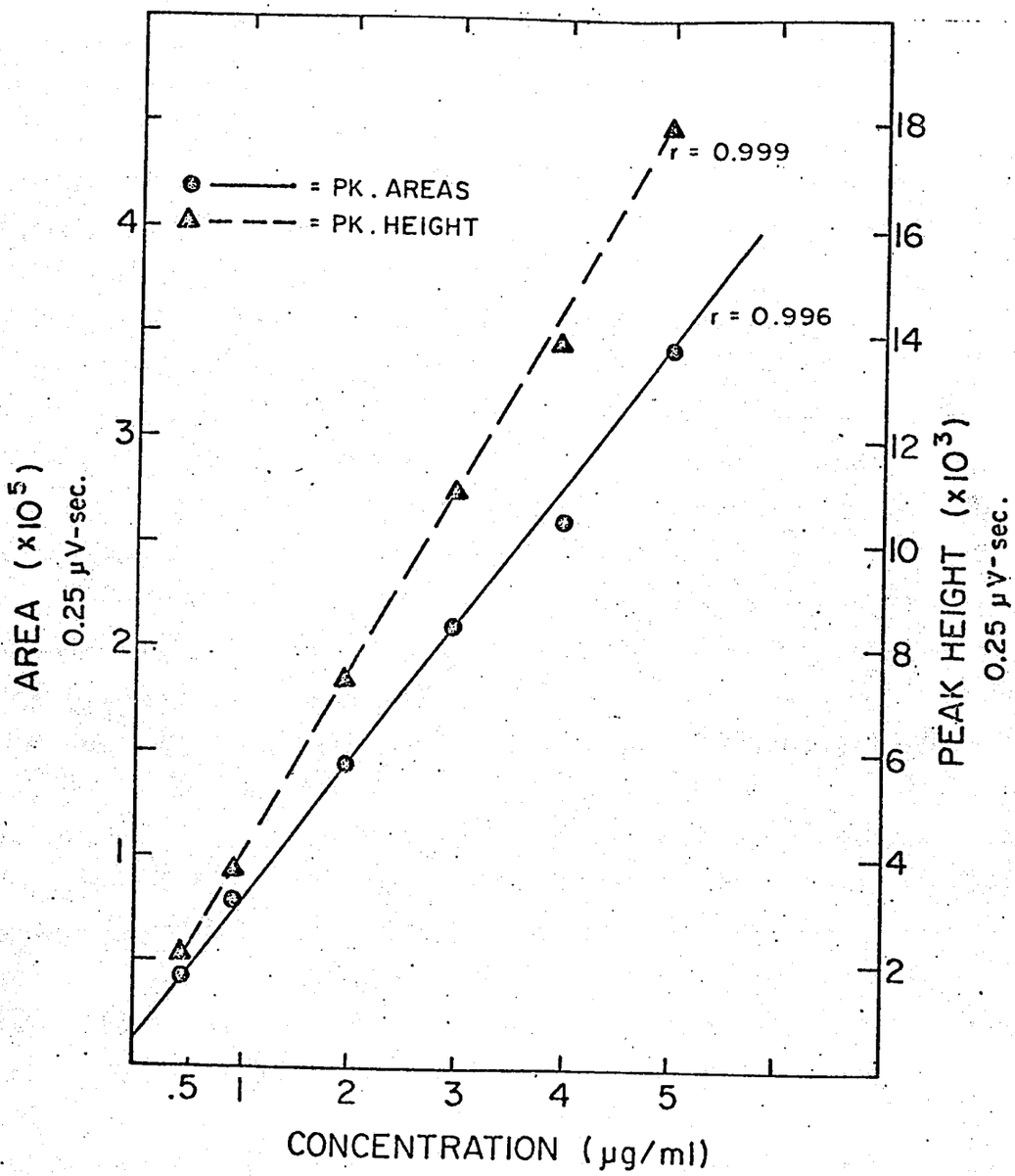


Figure 3a. GC calibration curve for standard solutions of acetone cyanohydrin in ethyl acetate (0.5-5 μg/ml)
Injection volume = 5μl Detector : NPD

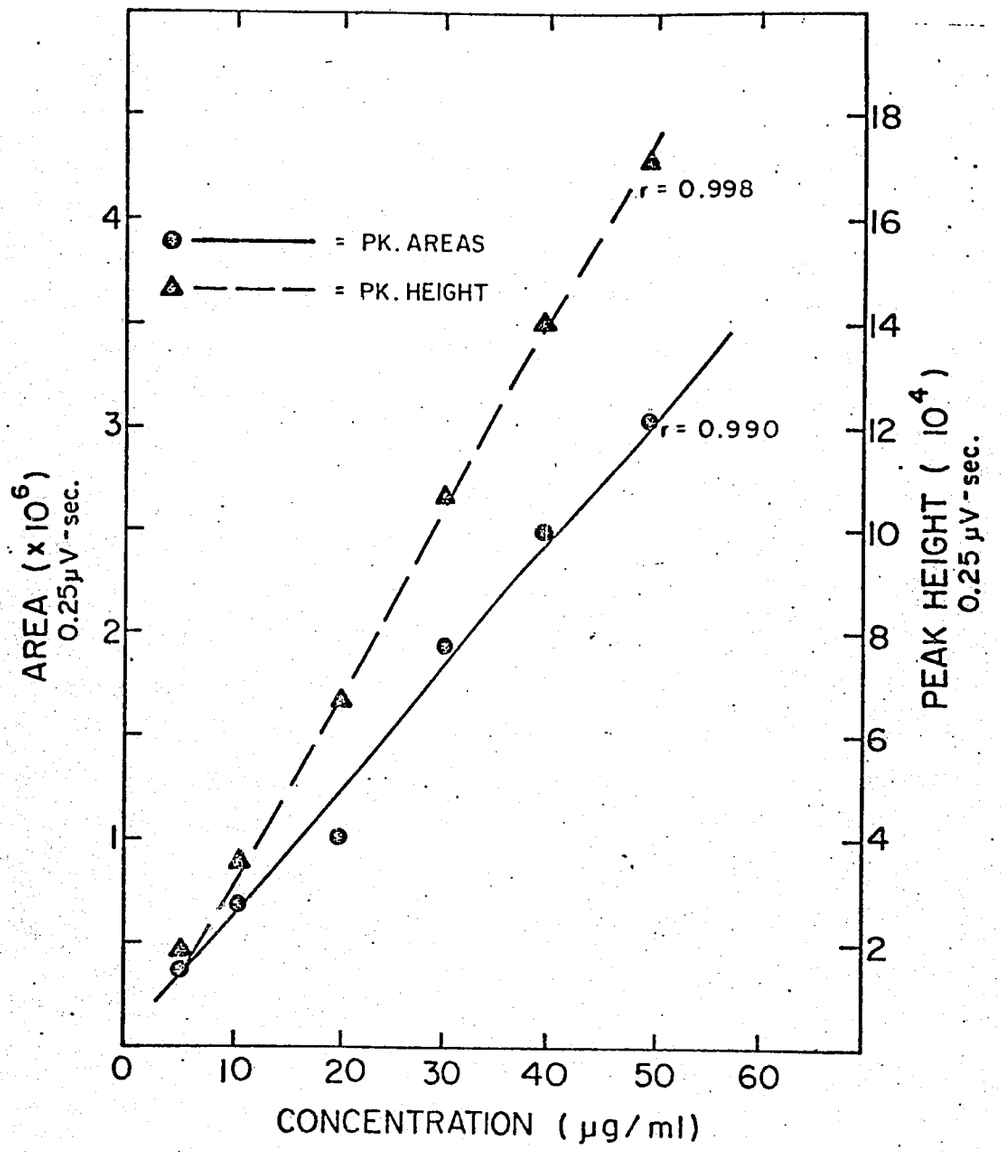


Figure 3b. GC calibration curve for standard solutions of acetone cyanohydrin in ethyl acetate (5–50μg/ml)
Injection volume = 5μl Detector : NPD

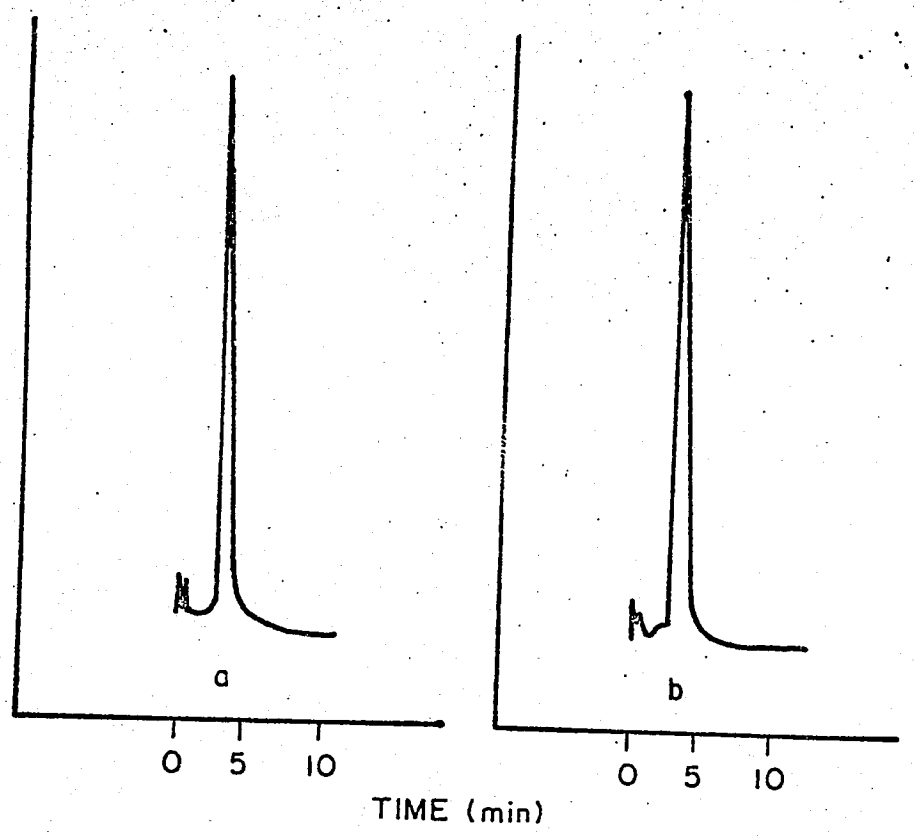


Figure 4. Chromatograms of (a) 100 ppm acetone cyanohydrin in ethyl acetate (b) 100 ppm actone cyanohydrin + 100 ppm acetone, 100ppm methanol, 100ppm methyl methacrylate on OV-17 column.

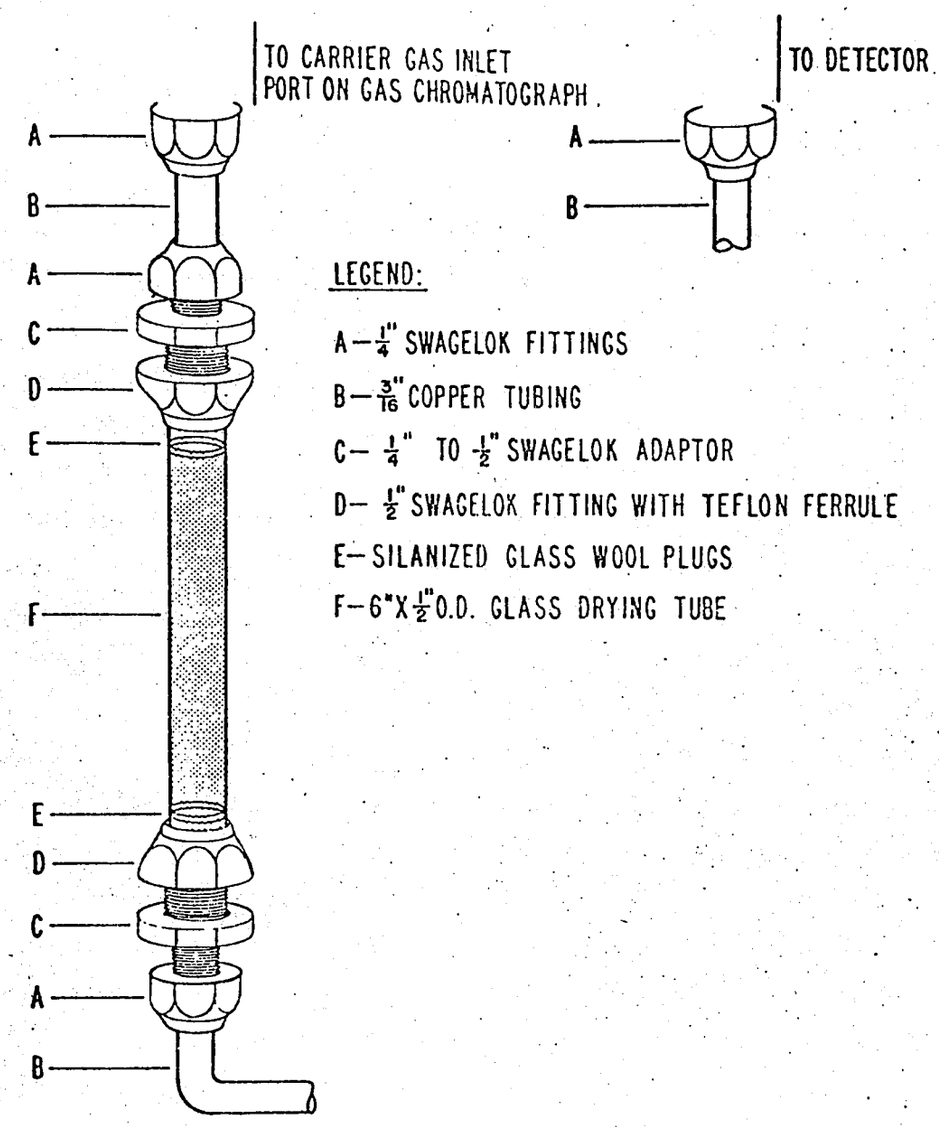


Figure 5. Purging system for porous polymers.

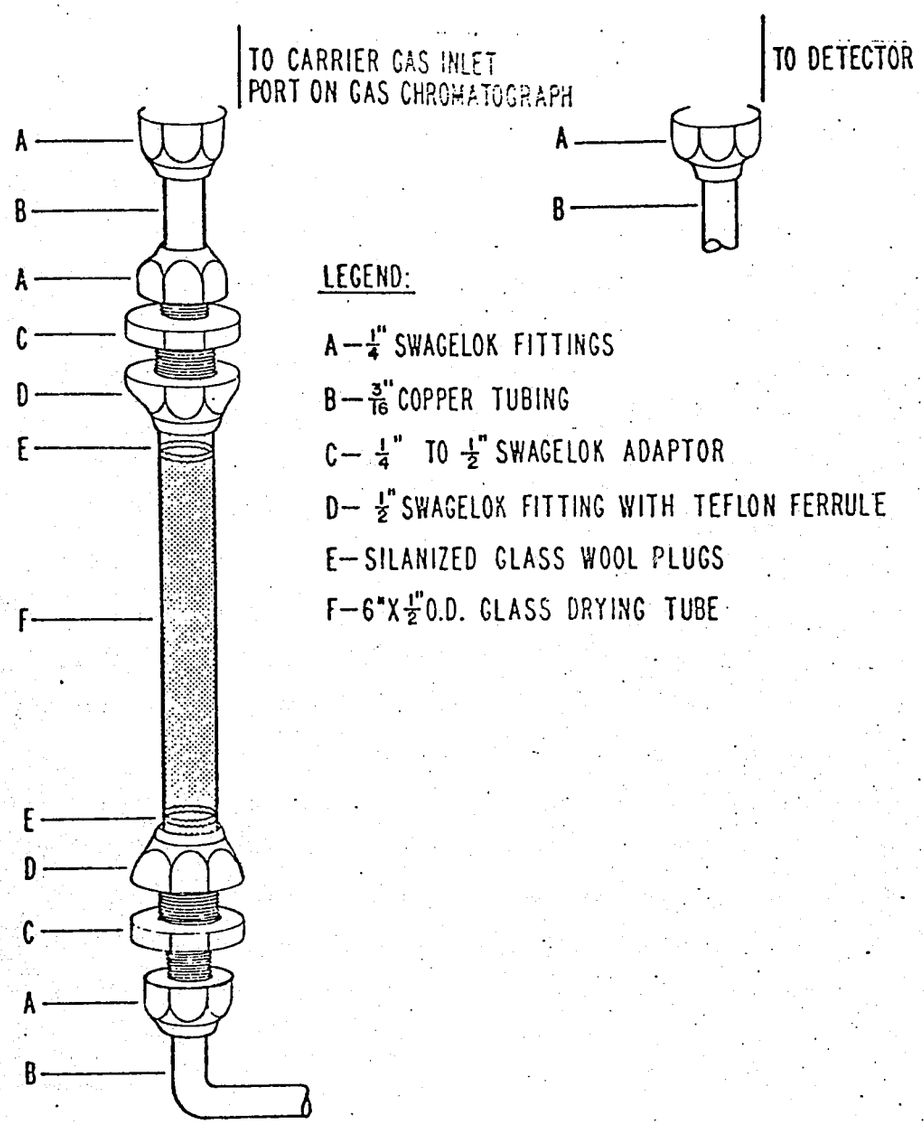


Figure 5. Purging system for porous polymers.

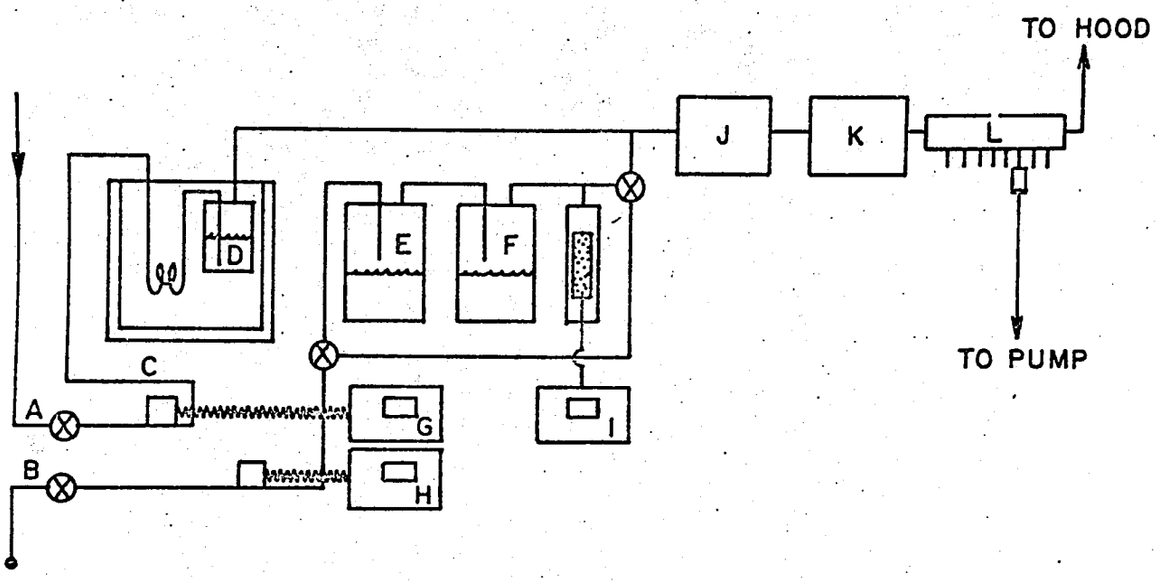


Figure 6. Generation system for acetone cyanohydrin.

APPENDIX A

ACETONE CYANOHYDRIN

Methods Research Branch

Analytical Method

Analyte:	Acetone Cyanohydrin	Method No.:	P&CAM 340
Matrix:	Air	Range:	0.33-16.7 mg/m^3 for a 3-L sample
Procedure:	Adsorption on Porapak QS, desorption with ethyl acetate, GC analysis via NPD	Precision:	0.093
Date Issued:			
Date Revised:		Classification:	E (Proposed)

1. Synopsis

A known amount of air is drawn through a sorbent tube containing Porapak QS to trap the analyte present. The Porapak QS is transferred to a small stoppered sample container and the analyte is desorbed with ethyl acetate. An aliquot of the resulting solution is injected into a gas chromatograph equipped with a nitrogen-phosphorous detector. The area of the resulting peak is determined and compared with areas obtained from the injection of standards.

2. Working Range, Sensitivity and Detection Limit

2.1 The method was evaluated by collecting 1-50 µg of acetone cyanohydrin at 0.2 L/min from U-tubes onto sorbent tubes containing Porapak QS over a one-hour period. The sample tubes were then exposed to humid air (relative humidity = 80%) at a temperature and pressure of 22°C and 740 torr for 15 minutes at 0.2 L/min.

2.2 The upper limit of the method is dependent upon the capacity of the Porapak QS to retain the analyte. A 1.0% weight breakthrough was observed when 100 µg of the analyte in 12 L of humid air (relative humidity = 80%) was collected onto a 100-mg bed of the sorbent at 0.2 L/min.

2.3 Levels as low as 0.1 µg/mL in ethyl acetate were analyzed using a nitrogen-phosphorous detector. At this level the precision of replicate injections was 5.3%.

3. Interferences

3.1 Any compound which has the same retention time as the analyte at the operating conditions described in this method is an interference. Using a nitrogen-phosphorous thermionic detector, the following compounds have been found not to interfere with the analysis of acetone cyanohydrin: methanol, acetone, and methyl methacrylate. Retention time data on a single column cannot be considered as proof of chemical identity.

3.2 The analyte decomposes readily in the presence of water vapor. Since Porapak QS has an apparent capacity to collect water, it is necessary to refrigerate all samples collected from humid atmospheres immediately after sampling is completed. Tests have shown that samples of the analyte that have been spiked via evaporation from U-tubes onto sampling tubes containing the sorbent and exposed to 3 L of humid air (relative humidity = 80%) are stable for at least 5-7 days, if stored at 0°C.

4. Precision and Accuracy

4.1 The pooled relative standard deviation for the total sampling and analytical method in the range 0.33-16.7 mg/m^3 was 9.3%. At the 0.33 mg/m^3 level, this corresponds to a standard deviation of 0.031 mg/m^3. A 5% variation in pump flow is assumed in computing the pooled relative standard deviation.

4.2 Storage samples were collected from U-tubes and exposed to humid air for 15 minutes at 0.2 L/min. These samples were stored for periods ranging from 1 to 5 or 7 days. The 1-day samples were stored at ambient temperatures. The longer-term storage samples were maintained at 0°C. There was no statistical difference at the 95% level of confidence between the averages for the two groups.

5. Advantages and Disadvantages

5.1 This method was developed for monitoring personal exposures. However, it has not been field tested.

5.2 Data suggest that at least 12 L of humid air can be sampled without danger of breakthrough of acetone cyanohydrin. However, when the amount of the cyanohydrin found on the backup section of the sampling tube exceeds 10% of that found on the front section, the probability of sample loss exists.

5.3 The samples must be refrigerated at 0°C as soon as possible after collection to prevent degradation of the analyte by co-adsorbed water vapor.

5.4 The precision of the method is limited by the reproducibility of the pressure drop across the sorbent tube. This variation will affect the flow and cause the volume to be imprecise, because the pump is usually calibrated for one tube only.

6. Apparatus

6.1 Personal sampling pump capable of sampling at 0.2 L/min. The pump should be calibrated with a representative Porapak QS tube in line.

6.2 Porapak QS tube. Glass tube, 7.0-cm long, 6-mm outside diameter, and 4 mm-inside diameter, containing 100-mg front and 50-mg backup sections of 50/80 mesh pre-extracted Porapak QS. The sorbent beds are separated by a 2-mm portion of silanized glass wool and contained at the ends by silanized glass wool plugs. Prior to use, the sorbent is extracted with acetone-methanol (80/20, v/v) in a Sohxlet apparatus for four hours, extracted with hexane for one hour, and allowed to air dry. Several grams are then placed in the drying tube of the apparatus shown in Figure 1. This apparatus is connected to the carrier gas inlet port of a GC oven and exhausted into the detector. The sorbent is dried at 120°C under helium flowing at approximately 20 mL/min for two hours, then allowed to cool in a clean desiccator. Care should be taken to avoid excessive agitation of the Porapak QS during handling. A static charge can be induced in the material and is not readily dissipated. This will cause the individual particles to agglomerate, making the material difficult to handle while packing the collection tubes. The glass tubes should be washed with acetone and thoroughly dried prior to packing with Porapak QS. This prevents the sorbent from adhering to the tube walls. Cap the sorbent tubes with plastic caps prior to use.

6.3 Gas chromatograph equipped with a nitrogen-phosphorous detector. The transfer lines from the injector to the column and from the column to the detector must be replaced with teflon tubing (as described in Figure 2).

6.4 GC column, 2-m long x 4-mm inside diameter teflon tubing packed with 5% OV-17 on Chromosorb T (40/60 mesh). The packing is prepared and loaded into the column using the techniques

*Porapak QS is a co-polymer of styrene-divinylbenzene which has been treated with a silylating agent. It is manufactured by Waters Associates.

described in Reference 2. The portion of the column to be inserted into the injection port should remain empty to preclude crushing the soft Teflon support and thereby plugging the front-end of the column.

6.5 Electronic integrator or some other suitable method of determining peak areas.

6.6 Vials, 2-mL, with glass stoppers or teflon-lined caps.

6.7 Microliter syringes, 10-µL and other convenient sizes, for preparing standards.

6.8 Pipets, delivery type, 10-mL and other convenient sizes.

6.9 Volumetric flasks, 10-mL and other convenient sizes, for preparing standard solutions.

6.10 Stopwatch.

6.11 Manometer.

6.12 Sohxlet extractor.

6.13 Parafilm.

6.14 Glass tubes, 7-cm x 4-mm i.d., flame-sealed at one end, used for desorption experiments.

6.15 Portable refrigerant, such as Koolit (PDC Pkg., Medford, MA), for refrigerating samples during shipment.

7. Reagents

7.1 Acetone, chromatoquality.

7.2 Acetone cyanohydrin, 98+% purity (Aldrich Chemical Co.).

7.3 Ethyl acetate, distilled in glass.

7.4 Nitrogen, purified.

7.5 Hydrogen, prepurified.

7.6 Air, filtered, compressed.

7.7 Hexane, distilled in glass.

7.8 Methanol, distilled in glass.

8. Procedure

8.1 Cleaning of Equipment. Wash all glassware used for the laboratory analysis with detergent. Thoroughly rinse with tap water and distilled water. Allow to dry.

8.2 Collection and Shipping of Samples

8.2.1 Immediately before sampling, remove the caps from the ends of the tube. All tubes must be packed with Porapak QS from the same manufacturer's lot.

8.2.2 Connect the Porapak QS tube to the sampling pump with a piece of flexible plastic tubing. The smaller section of the Porapak QS tube is used as a backup and is positioned nearer the sampling pump.

8.2.3 Place the tube in a vertical position during sampling to minimize channeling through the Porapak QS.

8.2.4 Do not permit air being sampled to pass through any hose or tubing before entering the Porapak QS tube.

8.2.5 Sample 3 L of air at 0.2 L/min over a 15-minute period. At least 12 L of air can be sampled. Record the sampling time and the flowrate.

8.2.6 Record the temperature, pressure and relative humidity of the atmosphere being sampled. If the pressure reading is not available, record the elevation.

8.2.7 Seal the Porapak QS tube with plastic caps immediately after sampling. Do not use rubber caps.

8.2.8 With each batch of ten samples, submit at least one blank tube made from the same lot of Porapak QS as used for sample collection. This tube is subjected to exactly the same handling as the samples (uncap, seal, transport) except that no air is drawn through it.

8.2.9 Pack the capped tubes tightly. Pad them before they are shipped to minimize tube breakage. Ship the samples in an insulated container containing a portable refrigerant. Maintain the temperature at 0°C.

8.2.10 Any samples of bulk material should be submitted to the laboratory in glass containers with a teflon-lined cap. These samples should not be transported in the same container as the Porapak QS tubes.

8.2.11 Refrigerate the Porapak QS tubes at 0°C as soon after sampling as possible.

8.3 Analysis of Samples

8.3.1 Preparation of Samples. Remove the plastic cap from the inlet end of the Porapak QS tube. Remove the glass wool plug and transfer the first (larger) section of sorbent to a 2-mL vial. Desorb the front glass wool plug with the front sorbent section. Remove the separating section of silanized glass wool and transfer the backup section of Porapak QS to another stoppered vial. Desorb the separating glass wool section with the backup sorbent. It may be necessary to tap the tube sharply to affect complete transfer of the Porapak QS. Analyze the two sections separately.

8.3.2 Desorption of Samples. Pipette 1.0 mL of ethyl acetate into each sample container. Allow samples to desorb in an ultrasonic bath for one hour. Analyses should be completed the same day that the samples are desorbed.

8.3.3 GC Conditions

	Flow Rates (mL/min)
Carrier gas (N_2)	33
Hydrogen	5
Air	175
	Temperatures (°C)
Injector	100
Detector	100
Column	70

The analyte has a retention time of approximately 3 minutes under these conditions using the column recommended in Section 6.4. The ethyl acetate will elute from the column before the analyte.

8.3.4 Injection. Inject a 5-μL aliquot into the gas chromatograph using the solvent-flush technique. It may not be advisable to use an automatic sample injector because of possible plugging of the syringe needle with Porapak QS particles.

8.3.5 Measure the area of the sample peak with an electronic integrator or some other suitable form of area measurement.

8.4 Determination of Desorption Efficiency

8.4.1 The desorption efficiency of acetone cyanohydrin may vary from one laboratory to another and, also, from one batch of Porapak QS to another. Thus, it is necessary to determine the desorption efficiency for each batch of Porapak QS used.

8.4.2 One hundred milligrams of Porapak QS is measured into a sample vial or a 7-cm x 4-mm i.d. glass tube, flame-sealed at one end. This Porapak QS must be from the same batch as that used in obtaining the samples. The open end is capped with Parafilm. A known amount of an ethyl acetate solution containing 1-10 µg/µL of acetone cyanohydrin is injected directly onto the Porapak QS bed with a microliter syringe and the vial is capped with parafilm. The amount injected is equivalent to that present in an air sample at a selected level.

Six vials at each of three levels covering the range of interest are prepared in this manner and allowed to stand overnight to assure complete adsorption of the acetone cyanohydrin onto the Porapak QS. A parallel blank tube should be treated in the same manner except that no sample is added to it. The sample and blank tubes are desorbed and analyzed as described in Section 8.3.

Prepare the standards by injecting the same volume of acetone cyanohydrin solutions into 1.0 mL of ethyl acetate with the same syringe as used in the preparation of the samples. These are analyzed with the samples.

The desorption efficiency (D) equals the average weight of acetone cyanohydrin in µg recovered from the tube (Q_r) divided by the weight in µg added to the tube (Q_a).

$$D = \frac{Q_r}{Q_a}$$

If D varies significantly with sample weight, plot D vs. Q_r and use the curve to correct for adsorption losses in Section 10.4.

9. Calibration and Standardization

9.1 Prepare a stock standard solution containing 10 µg/µL of acetone cyanohydrin in ethyl acetate.

9.2 From the stock solution, prepare at least five standards to cover the range 0.5-100 µg in 1.0 mL of ethyl acetate.

9.3 Analyze the standards with the samples.

9.4 Prepare a calibration curve by plotting the weight in µg of acetone cyanohydrin in the sample versus peak area.

10. Calculations

10.1 Read the weight in µg corresponding to each peak area from the standard curve.

10.2 No response from the blank is expected. If the blank is significant, determine its source and eliminate or correct for it.

10.3 Add the weights found in the front and backup sections to determine the total weight of the sample.

10.4 If the desorption efficiency (D) is determined to be significantly different from 1.0 (Section 8.4.2), divide the total weight (W) by the desorption efficiency to obtain the corrected weight in µg (W_C).

$$W_C = \frac{W}{D}$$

10.5 The concentration (C) of acetone cyanohydrin in the air sampled can be expressed in µg/L as follows:

$$C = \frac{W_C}{V}$$

where: V = volume of air sampled in liters (L).

This number is numerically equal to the concentration of acetone cyanohydrin in mg/m^3.

10.6 C may be converted to the concentration in ppm (C') by use of the following formula:

$$C' = C \times \frac{24.45}{M} \times \frac{760}{P} \times \frac{T + 273}{298}$$

where: P = the pressure of air sampled in torr
T = the temperature of air sampled in °C
24.45 = the molar volume of an ideal gas in liters (L)
M = molecular weight (g/mole) of acetone cyanohydrin (85 g/mole)
760 = standard pressure in torr
298 = standard temperature in °K

11. References

11.1 R. A. Glaser and P. M. Fey. Development of a Quantitative Sampling and Analytical Method for Acetone Cyanohydrin. Report of research performed during fiscal years 1979 and 1980.

11.2 Supina, W. R. "The Packed Column in Gas Chromatography," Supelco Inc., Bellefonte, PA, 1974, pp. 91-94.

Robert A. Glaser
Paula M. Fey
Organic Methods Development Section

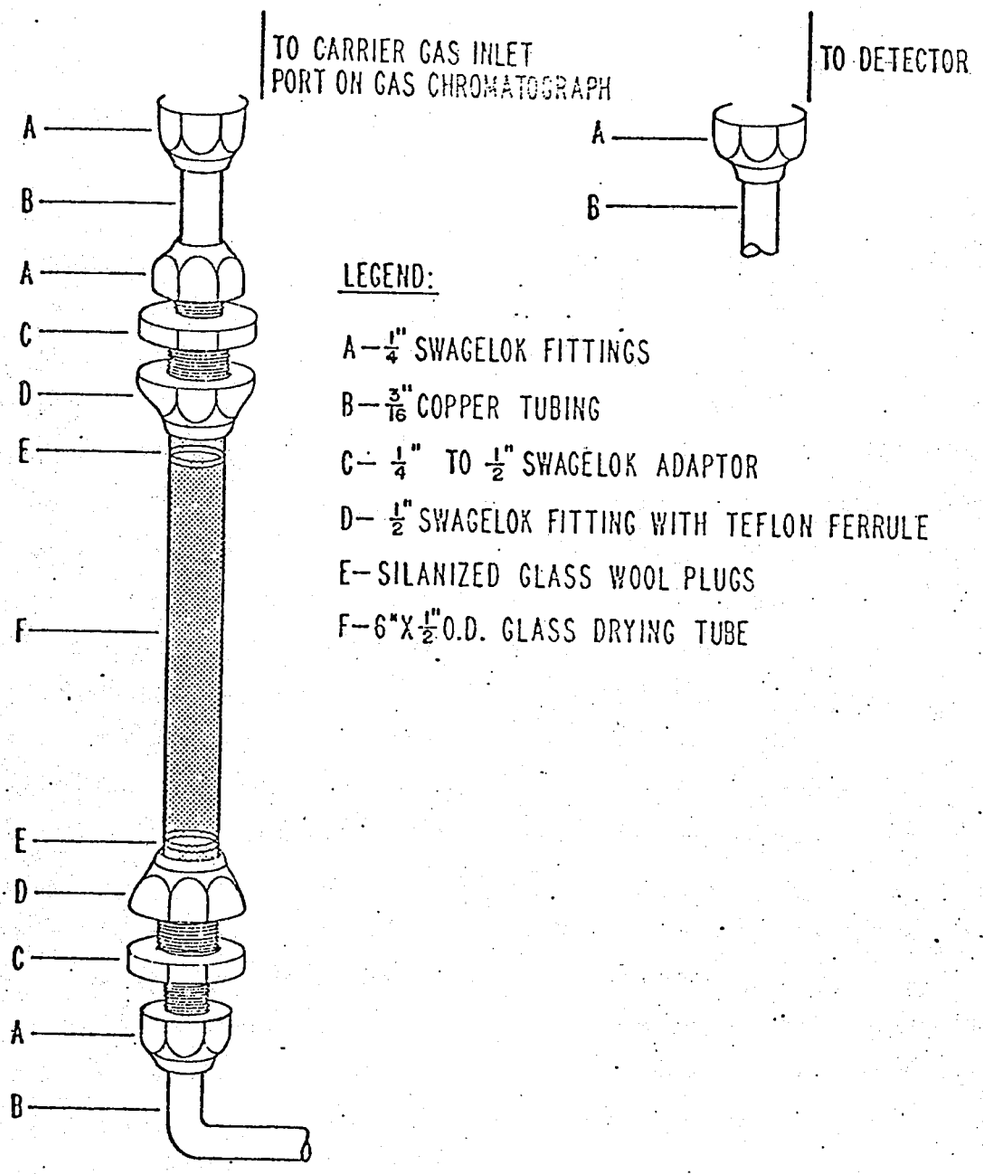

TO CARRIER GAS INLET PORT ON GAS CHROMATOGRAPH
TO DETECTOR
A
B
A
C
D
E
F
E
D
C
A
B
A
B
LEGEND:
A—1/4" SWAGELOK FITTINGS
B—3/16" COPPER TUBING
C— 1/4" TO 1/2" SWAGELOK ADAPTOR
D— 1/2" SWAGELOK FITTING WITH TEFLON FERRULE
E—SILANIZED GLASS WOOL PLUGS
F—6"X1/2"O.D. GLASS DRYING TUBE

Figure 1.

Figure 2. All Teflon gas chromatographic system used for the analysis of acetone cyanohydrin.