

## A GAS-CHROMATOGRAPHIC METHOD FOR THE PREPARATION OF $^{14}\text{C}$ -LABELED VINYL CHLORIDE

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Received on June 6, 1975.  
Revised on August 7, 1975.

### SUMMARY

*A modification of our previously reported<sup>2</sup> gas chromatographic method of preparing vinyl- $^{14}\text{C}_2$  chloride ( $^{14}\text{C}$ -VC) has been made. The procedure using 1,2-dichloroethane- $^{14}\text{C}_2$  obtained from New England Nuclear Corporation gave good yields of  $^{14}\text{C}$ -VC as a gas mixture with helium.*

*The radiochemical purity of a representative sample of the  $^{14}\text{C}$ -VC was determined by gas chromatography. Sequential fractions were trapped from gas chromatographic columns in a toluene based liquid scintillator. The radioactivity-time profile was correlated with the retention time of authentic VC gas. A mass spectrum and a high resolution infrared spectrum obtained on the same sample of  $^{14}\text{C}$ -VC were identical to spectra of authentic VC. The major radioactive impurity appeared to be acetylene.*

### INTRODUCTION

Exposure to high levels of vinyl chloride has been implicated as the cause of liver cancer in some industrial workers and for this reason there has been a great interest in understanding the metabolism of this important chemical. To facilitate these studies  $^{14}\text{C}$ -labeled vinyl chloride ( $^{14}\text{C}$ -VC) was required, but commercially prepared  $^{14}\text{C}$ -labeled samples polymerized on storage and were not usable. A convenient and direct method for synthesis of the radioactive vinyl chloride was needed so that the preparation could be made quickly, just prior to each use.

The literature describes the dehydrohalogenation of 1,2-dichloroethane over a carbon catalyst at elevated temperatures<sup>1</sup>, and we have previously found that by modifying a glass preparative gas chromatographic column to make this conversion, one can use it as a convenient generator of

$^{14}\text{C-VC}^2$ . The precursor is 1,2-dichloroethane- $^{14}\text{C}_2$ , ( $^{14}\text{C-DCE}$ ) which is stable, relatively inexpensive, and commercially available. This present report details an analytical size column that has proved adequate for repeated use and is somewhat more convenient. Experiments are also reported which establish the radiochemical and chemical purity of the synthesized  $^{14}\text{C-VC}$ .

## MATERIALS AND METHODS

### Gas Chromatograph Column

To allow adaptation to a Hewlett Packard model 5750 gas chromatograph, a glass column was prepared. The large separation coil was 2.4 m long and the smaller pyrolysis coil was 90 cm in length. The inside diameter of the tubing was 3 mm. The large coil was packed with 80-90 mesh 25% Dow Corning 410 Gum on Chromosorb W (acid washed). The small coil was packed with a charcoal mixture prepared by mixing 20 g Chromosorb W and 10 g Darco G-60 charcoal powder. This catalyst section was then fitted with an external thermocouple and wrapped with asbestos tape. Around this tape was wound asbestos covered Chromel A wire (22 gauge) and then a final covering of asbestos tape for insulation. The heating wires were connected to a variable transformer to allow independent heating of the pyrolyzer portion of the column.

The column could then be conveniently connected to the metal liner tube in the injection port and the terminal end connected to the thermal conductivity detector. It was heated at 200°C overnight before use. During operation no heat was applied to the column and the lid to the column oven was maintained open to keep the column at 30-50°C. The pyrolysis coil was heated to 470-480°C. Samples of up to 10  $\mu\text{l}$  of DCE were injected neat. Detector and injection port temperatures were varied from 100 to 300°C with no apparent differences observed. The exit port of the chromatograph was modified to connect to a 100 ml syringe which was fitted with a stainless steel stopcock. The vinyl chloride peak was collected, the stopcock closed and the syringe removed.

### Radiochemical Purity Determination

Vinyl chloride (Matheson Gas Products, Joliet, Ill.) of 99.9% minimum purity was used as an authentic gas standard for comparison to the synthesized  $^{14}\text{C}$  material.

1,2-dichloroethane- $^{14}\text{C}_2$ , ( $^{14}\text{C-DCE}$ ) was purchased from the New England Nuclear Co. (Boston, Mass.). The specific activity of the  $^{14}\text{C-DCE}$  (lot # 819-021) was 3.4 mCi/mole. The purity reported by New England Nuclear was >97% as determined by ratio of gas chromatographic peak area measurements. Six microliters (liquid) of  $^{14}\text{C-DCE}$  was injected

on the synthesis column and the  $^{14}\text{C}$ -VC produced was collected in a total volume of 40 ml with an airtight glass syringe.

One milliliter aliquots of the  $^{14}\text{C}$ -VC ( $4.332 \times 10^6$  DPM) were analyzed by gas chromatography (Hewlett-Packard, Model 5750) on two different columns (Porapak Q, 20% Carbowax 20M). Table I gives the specific conditions of the analysis. The effluent gases, after passing through the thermal conductivity detector, were trapped by bubbling directly into scintillation vials containing 20 ml of scintillator. The scintillator consisted of Concifluor (Mallinckrodt Chemical Works, St. Louis, Missouri), 2-methoxyethanol, and toluene (1:1.8:11). The vials were changed every 15 seconds for 9 minutes. The efficiency of trapping VC by bubbling through toluene had been checked in this laboratory previously and shown to be 90% efficient. The radioactivity in the various fractions was determined by counting with a Nuclear Chicago Mark II liquid scintillation spectrometer. External standard channels ratio was used to determine the counting efficiency.

Additional aliquots of the  $^{14}\text{C}$ -VC were subjected to GC-MS analysis (Finnigan Quadrupole GC-MS, Sunnyvale, Ca.) and infrared spectrometry (FTS-14, Digilab, Cambridge, Mass.). Table I also gives conditions of

TABLE I  
Conditions of GC and GC-MS Analysis

Instrument	Finnigan Quadrupole GC-MS	Hewlett-Packard GC	Hewlett-Packard GC
Col. Type	Porapak Q (80/100 mesh)	Porapak Q (80/100 mesh)	20% Carbowax 20M (60/80 mesh on Chromosorb W, AW)
Col. Dimensions	6' x 1/4" stainless steel	5' x 1/4" stainless steel	10' x 1/4" stainless steel
Detector	Mass Spectrometer	Thermal Conductivity	Thermal Conductivity
Col. Oven Temp ( $^{\circ}\text{C}$ )	100-200, 30/min.	150	60
Injection Temp ( $^{\circ}\text{C}$ )	250	270	270
Thermal Conductivity Detector Temp ( $^{\circ}\text{C}$ )		100	100
Bridge Current		150 mA	150 mA
Flow Rate	14 (Rotometer)	20 ml/min.	20 ml/min.
Separator Vacuum	$5 \times 10^{-1}$ torr		
Source Vacuum	$5 \times 10^{-5}$ torr		
Separator Temp ( $^{\circ}\text{C}$ )	220		
Ion Source Temp ( $^{\circ}\text{C}$ )	40		
Ion Energy	70 eV		
Retention Time Standard VCM (sec)	150	313	259

the GC-MS analysis. Infrared analysis was conducted by introducing the  $^{14}\text{C}$ -VC into an evacuated 10 cm gas cell. The infrared spectrum was recorded at a pressure of 150 Torr in a normal and expanded mode to detect small quantities of impurities.

## RESULTS AND DISCUSSION

### The Generator

The  $^{14}\text{C}$ -VC generator was modified to fit an analytical gas chromatograph. In addition to the advantage of a smaller apparatus size, this change allowed the use of a thermal conductivity detector which revealed

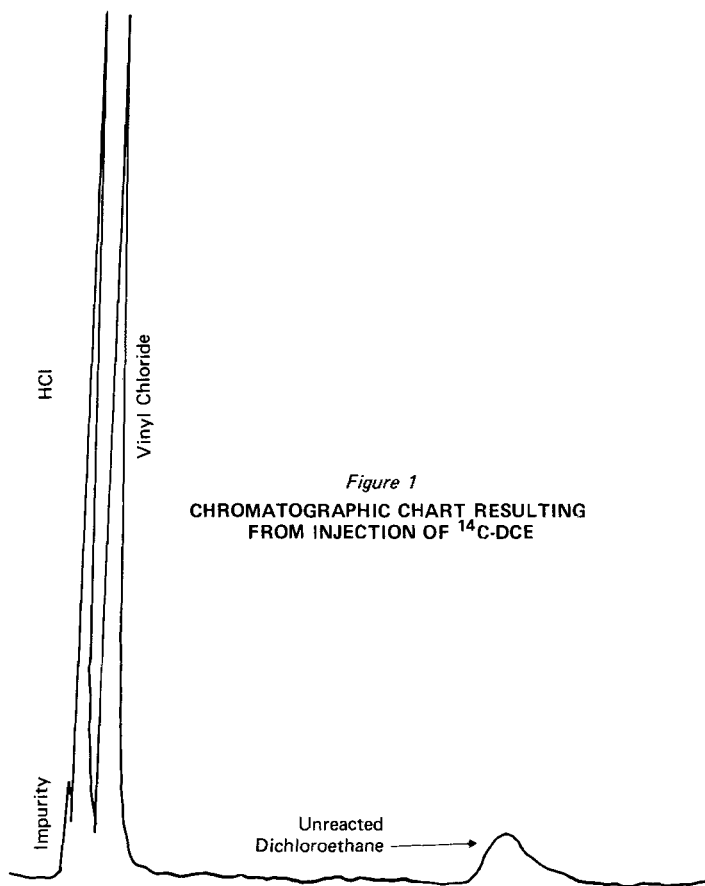


Figure 1  
CHROMATOGRAPHIC CHART RESULTING  
FROM INJECTION OF  $^{14}\text{C}$ -DCE

the HCL by-product and did not result in product loss due to stream splitting.

Injection of 10  $\mu\text{l}$  samples of dichloroethane on the column with

the dehydrohalogenation reactor portion at  $470^{\circ}\text{C}$ , the separation column at ambient temperature, and a helium carrier gas flow rate of about 30 ml per min., produced 4 peaks in the thermal conductivity detector (see Figure 1). The first, though minor component, appeared at approximately 2 minutes. The second peak was HCl with a retention time of 2.3 min. and this was followed by a nearly equivalent vinyl chloride peak at 3.3 minutes. Any unreacted DCE could be detected much later.

No attempt was made to determine the maximum load of dichloroethane that could be used, but the yield of vinyl chloride obtained in the conversion was determined by several factors, the first being the amount of dichloroethane injected. No doubt a maximum percent conversion point could be reached, but this was not determined. A second factor in the converted yield was the temperature of the dehydrohalogenator portion. As the temperature was increased above  $350^{\circ}\text{C}$ , the percent yield of vinyl chloride increased with a slight concomitant increase in the by-product peak and of course the HCl. A third factor controlling the yield was the helium flow rate and like the others, this showed a direct relationship to the time the gas remained in the reaction chamber.

The yield of  $^{14}\text{C}$ -VC after injection of  $5.5\ \mu\text{l}$   $^{14}\text{C}$ -DCE was 46% as expressed on a mole basis. The yield was determined by analyzing the  $^{14}\text{C}$ -VC by gas chromatography. The collection interval for the VC was determined by the response of the thermal conductivity detector to the synthesized VC (Figure 1). To insure a high concentration of VC with minimal radiochemical contamination, only the central portion of the product peak was collected; therefore, the 46% yield actually represents a minimum value under the stated conditions.

The specific activity of the  $^{14}\text{C}$ -VC was 2.7 mCi/mmoles. This specific activity was determined by analyzing an aliquot (1 ml) of the  $^{14}\text{C}$ -VC by gas chromatography and by determining the  $^{14}\text{C}$ -activity by counting aliquots (0.1 ml) prepared by bubbling the VC into open scintillation vials containing a toluene based scintillant. The discrepancy between the specific activity of  $^{14}\text{C}$ -VC and  $^{14}\text{C}$ -DCE, 2.7 versus 3.4 respectively, is somewhat large but it is likely that the methodology employed in determining the  $^{14}\text{C}$ -activity of the VC could result in an error of the present magnitude.

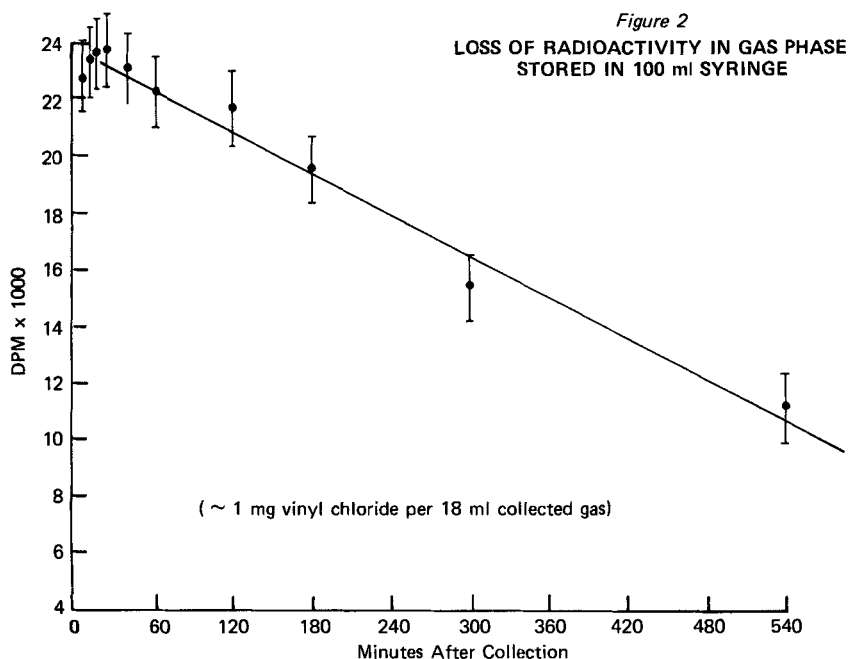
The separation of the HCl and vinyl chloride obtained from the chromatographic portion of the column was sufficient to allow each peak to be collected independently, however, the separation was not complete and the  $^{14}\text{C}$ -VC contained some HCl. It was found that one could remove the small amount of HCl present by partially filling the syringe with dilute aqueous caustic, displacing with the collected gas and then sampling the HCl-free vinyl chloride mixture from the gaseous portion.

This gas could presumably then be dried by passing through some drying agent. Alternately, one could collect the gas by bubbling through a solvent such as toluene or by trapping in a cold trap.

As reported previously,<sup>2</sup> the glass syringe collection system showed no loss of unlabeled vinyl chloride over several days. However, there was a loss of  $^{14}\text{C}$ -VC with time as seen in Figure 2. A simple measurement of the radioactivity of the vinyl chloride was made by bubbling an aliquot of the gas mixture through toluene based scintillation cocktail (Liquifluor® New England Nuclear). Direct counting of the solutions at various time intervals revealed the level of radioactivity in the gas phase to be relatively constant over a 2-3 hour period. After 9 hours it had decreased by 50%. One explanation for this loss could be polymerization of the vinyl chloride on the walls of the syringe and removal from the gas phase, since mechanical losses had been shown to be negligible. Attempts to wash the syringe to recover the lost activity were only marginally successful.

#### Radiochemical Analysis

The profile of radioactivity trapped from both gas chromatographic systems indicated that the  $^{14}\text{C}$ -VC constituted 97% (Porapak Q) and 96% (Carbowax) of the total radioactivity trapped from the respective columns. A  $^{14}\text{C}$  contaminant eluting prior to VC in both systems comprised from



1-2% of the radioactivity. The mean total radioactivity recovered was 98% of that applied. This was well within the limits of accuracy in measuring the 1 ml aliquot introduced onto the columns.

The total ion chromatogram (TIC) was obtained from the GC-MS analysis. Individual mass spectra of the peaks indicated the presence of  $\text{N}_2$ ,  $\text{CO}_2$ , acetylene, and VC. The ratio of peak areas of VC to acetylene was 70:1. The mass spectrum of the synthesized  $^{14}\text{C}$ -VC was identical with the spectrum of the authentic VC standard.

Fourier-transform infrared spectrophotometric analysis indicated that the synthesized  $^{14}\text{C}$ -VC was identical to a VC standard gas sample. Under the given conditions, there was no evidence for the presence of any contaminants. The data indicated that the procedure used to synthesize  $^{14}\text{C}$ -VC yields a product of 96-97% minimum radiochemical purity. Close inspection of the radioactivity-time profile, reveals that the retention time for the peak radioactivity was slightly longer than that of the VC standard. This may be due to a delay in transit through the thermal conductivity detector prior to trapping. This presumed artifact caused a slow "bleeding effect" of  $^{14}\text{C}$ -activity from the detector as evidenced by the tailing in the resultant VC peak. Since the radioactivity associated with  $^{14}\text{C}$ -VC was calculated over the time elution period of the standard gas, the radiochemical purity may actually be slightly higher than reported here due to this trapping artifact.

The  $^{14}\text{C}$ -labeled contaminant which eluted prior to VC in both GC systems appears to be  $^{14}\text{C}$ -acetylene. The VC/acetylene ratio of 70:1 would suggest a 1.4% acetylene content which coincides with the 1-2% radiochemical contamination. Due to the trapping artifact, it is not possible to state absolutely that acetylene is the major contaminant; however, it seems a very likely possibility based on the GC-MS data.

The infrared analysis did not confirm the presence of acetylene. However, the estimated concentration was below the detection limits under the specified conditions.

Although the previous report<sup>2</sup> indicated instability in the  $^{14}\text{C}$ -DCE which had been prepared from ethylenechlorohydrin 1-2- $^{14}\text{C}$ , we have found the  $^{14}\text{C}$ -DCE obtained from New England Nuclear Corporation to be stable over relatively long periods of time. There was no problem with stability of the  $^{14}\text{C}$ -VC over the time (1-2 hours) required to use the product.

#### ACKNOWLEDGEMENTS

This work was partially sponsored by the Manufacturing Chemists Assoc. The authors wish to thank John Thompson for the infrared analysis, and Gerry McGowan for instrumental assistance.

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