Determination of Carbaryl and Some Other Carbamates by Gas Chromatography

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A method for preparing derivatives of some aryl carbamates to provide stable compounds for gas chromatography entails initial reaction at 4° C. between the carbamate and acetic anhydride. The reaction is completed at 97° C. over a 30-minute period. Both temperature-programmed and isothermal results using a hydrogen flame detector are given. Carbon-14 detection is used for verification of results.

While most carbamates of low boiling aliphatic alcohols are thermally stable and can be gas-chromatographed without decomposition (Zielinski, 1965a, b, c), most *N*-methyl aryl carbamates dissociate (Zielinski, 1965c) to give the parent phenol and methyl isocyanate. Di-*N*-substituted aryl carbamates are thermally stable under conditions elaborated in this paper. As acetylation of nitrogen compounds has long been one of the more useful methods of producing derivatives, a method was developed for carbaryl (*N*-methyl-1-naphthyl carbamate). Several aryl compounds of current interest were used to define a technique for successful chromatography.

EXPERIMENTAL

Preparation of Acetyl Derivative of Carbaryl. When carbaryl was subjected to acetylation using acetic anhydride and pyridine or sodium acetate, the product contained 30 to 35% 1-naphthyl acetate in addition to the *N*-methyl-*N*-acetyl-1-naphthyl carbamate. The use of methanesulfonic acid gave satisfactory results when samples were prepared at 4° C. and allowed to stand at room temperature for 24 hours or raised to and maintained at 97° C. for 30 minutes. In both cases the acetic anhydride to carbaryl ratio was 20 to 1 for large samples (1 gram) and 200 to 1 for 1-mg. samples. The methanesulfonic acid catalyst to carbaryl ratio was 1 to 1 for larger samples and 5 to 1 for 1-mg. samples. The large samples were isolated by pouring the mixture over cracked ice and allowing it to stand with stirring until the acetic anhydride was consumed. The solid precipitate formed was filtered, washed with cold water, and dried. For isolation of samples too small to precipitate, the aqueous system was extracted with chloroform and the resulting solution dried by filtration through anhydrous sodium sulfate.

Two 1-gram samples prepared by these techniques were sent to Research and Development, Union Carbide Corp., South Charleston, W. Va., where the *N*-acetyl carbaryl structure was verified by infrared and NMR spectroscopy.

Similar, but less detailed, studies were carried out on other carbamates.

Gas Chromatography. Basic parameters for retention data for carbamate analysis were investigated for packed and open-tube columns. Packed column work was performed on a Barber-Colman 5000 chromatograph using packed glass columns, helium carrier gas, hydrogen flame detection, and a RAM (radioactive monitoring) system. All columns were 8 feet long and 5-mm. I.D. (Barber-Colman nominal specification); mesh sizes of solid supports were 80 to 100 or 100 to 120. Flow rate optimization for plate number was 120 ml. per minute determined experimentally. A 10 to 1 effluent splitter was used throughout the investigation. One part was delivered to the flame detector and 10 parts to the RAM detector. The RAM system consists of a copper oxide combustion unit, a Drierite or perchlorate drying tube, and a concentric tube proportional counting chamber. Propane, at 12 ml. per minute, was the quench gas.

For studies with open-tube columns a modified Beckman Thermotrac using helium as a carrier gas and hydrogen flame detection was used. Direct column injection was introduced and the hydrogen burner was placed at the outlet of the column. Flow control was maintained using a Moore variable feedback flow regulator.

Standard 1/8-inch O.D. refrigeration tubing was washed thoroughly with chloroform, acetone, and chloroform. A thin film of Carbowax 20 M was placed on the tube by gravity flow of chloroform solution until the columns were completely filled. Each column was then attached to a 30-p.s.i.g. air line and the solution forcibly ejected. Air flow was continued until the column was reasonably dry, but never for more than 1 hour. Table I gives the per cent solutions used and estimated film thicknesses, obtained from measurements of solution volume and column dimensions. While errors may be fairly large, the relative results are reasonable, based upon theory and literature for capillary columns (Scott and Hazeldean, 1960).

Best results were obtained for the carbamates using film thicknesses of 0.2 to 0.5 micron. Thinner films gave relatively few plates, probably because of incomplete coverage, and for thick films, temperatures too high for reasonable retention times were required. The columns were preconditioned at 200° C. with a helium flow of 20 ml.

Table I. Film Thickness of Carbowax 20 M in Open-Tube Columns as a Function of Solution Concentration

Film Thickness, Microns	20 M in Chloroform, W./V. %
0.2	0.5
0.5	1
1.0	2
5.0	5

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per minute. The columns performed well to temperatures of 250° C., but when operated at 275° C. for an hour or more they no longer performed efficiently.

Studies were conducted on a number of columns of various lengths, diameters, and materials. Freshly prepared copper columns gave the best results for l-naphthol. Stainless steel columns always gave asymmetric peaks for lightly loaded columns; however, breakdown of the column coating at high temperatures was not as detrimental. The diameter effects were principally those expected. Smaller diameter columns gave higher plate numbers, but could not be loaded with the same total volume of sample—i.e., solute, sample, etc. Inlet splitting was required for columns less than $^1/_8$-inch O.D. For $^1/_8$-inch O.D. columns, sample volumes of 5 μl. could be inected directly onto the column. Columns of 100, 150, and 200 feet were prepared for several film thicknesses. Optimum length for carbaryl determination seems to be 150 feet. Optimum flow conditions were found to lie at flows which gave an average velocity for the air peak (determined at high temperatures with methane) of 10 to 15 cm. per second.

RESULTS

Packed Columns. For small samples—i.e., 1-mg. of the carbamate reacted—1 μl. of the sample was injected without isolation from the reacting mixture. Under the conditions required for the nonquantitative aspects of gas chromatography this was satisfactory. For trace analysis in complex mixtures, it might be necessary to develop cleanup procedures depending upon the nature of the mixture and interfering compounds.

The results of a study of reaction conditions are given in Figures 1, 2, and 3. One milligram of l-naphthyl C^{14}-labeled carbaryl was added to a mixture of 200 μl. of acetic anhydride and 5 μl. of methanesulfonic acid at 4° C. When the carbaryl was completely dissolved, the solution was allowed to come to room temperature and stand for 90 minutes. One microliter was then chromatographed on an 8-foot column of 5% by weight SE-30 silicone on 80- to 100-mesh Gas Chrom Q at a helium flow of 115 ml. per minute. The column was temperature-programmed at a rate of 3° C. per minute from 100° to 220° C. The results are shown in Figure 1, where the solid line is radioactivity and dashed line is mass. The first peak (solid line) is l-naphthyl acetate, the hump or

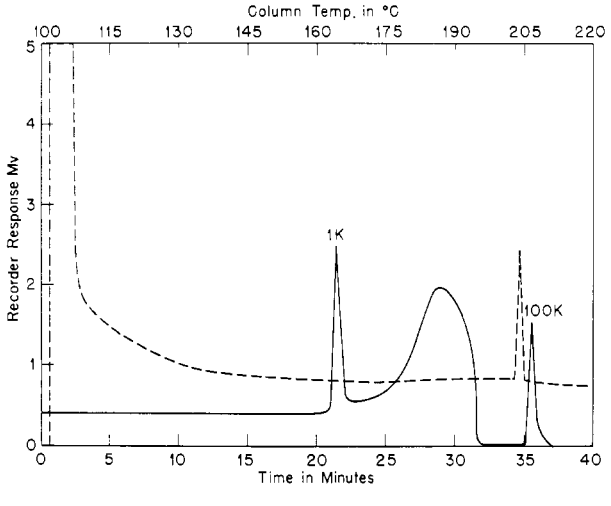

Figure 1. Chromatogram of *N*-acetyl carbaryl

Reactants mixed at 4° C., warmed to room temperature, and held 90 minutes

Column.	8 ft., 5-mm. I.D.
Support.	Gas Chrom Q, 80- to 100-mesh
Liquid phase.	5% SE-30
Flow rate, helium.	115 ml./min.
Injection port temp.	320° C.
Detector temp.	380° C.
Temp. program.	3° C./min.
Propane quench gas.	12 ml./min.

·····Mass
——C^{14}

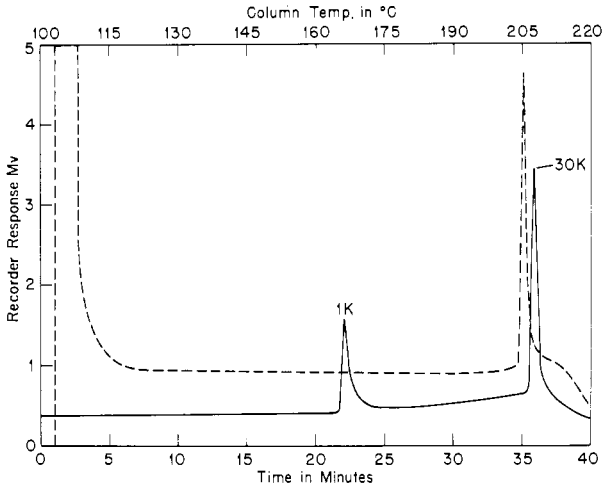

Figure 2. Chromatogram of *N*-acetyl carbaryl

Reactants mixed at 4° C., heated at 97° C. for 30 minutes
Chromatographic conditions same as Figure 1
·····Mass
——C^{14}

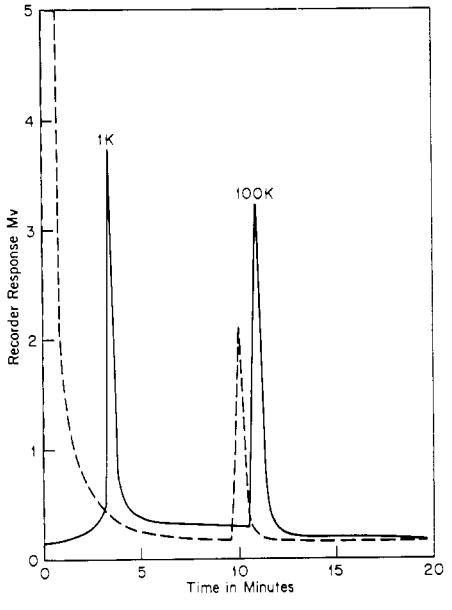

Figure 3. Isothermal chromatogram of *N*-acetyl carbaryl

Sample preparation of Figure 2

Column temp.	200° C.
Flow rate.	120 ml./min.
Other conditions.	Figure 1

·····Mass
——C^{14}

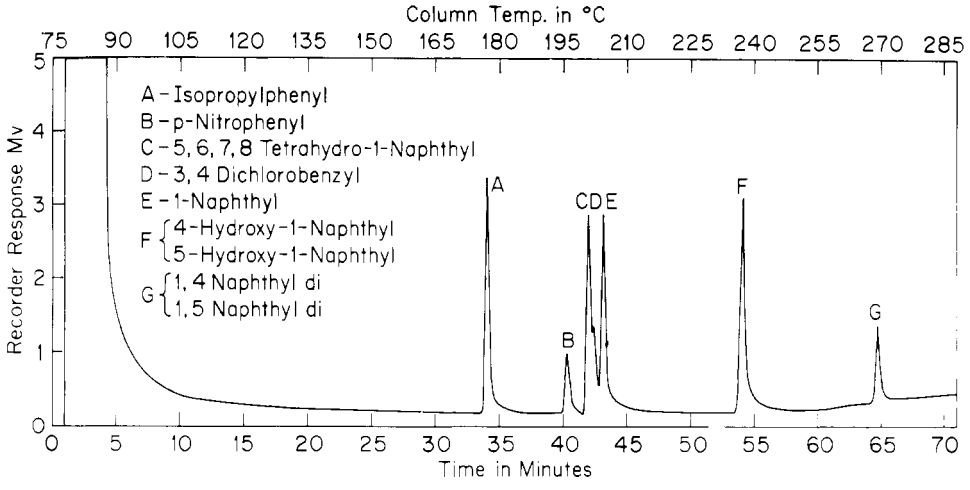

Figure 4. Chromatogram of *N*-methyl-*N*-acetyl carbamates on 5% SE-30

Injection port temp.	320° C.
Detector temp.	380° C.
Support.	Gas Chrom Q, 80- to 100-mesh
Column.	8 ft., 5-mm. I.D.
Flow rate, helium.	120 ml./min.
Temp. program.	3° C./min.

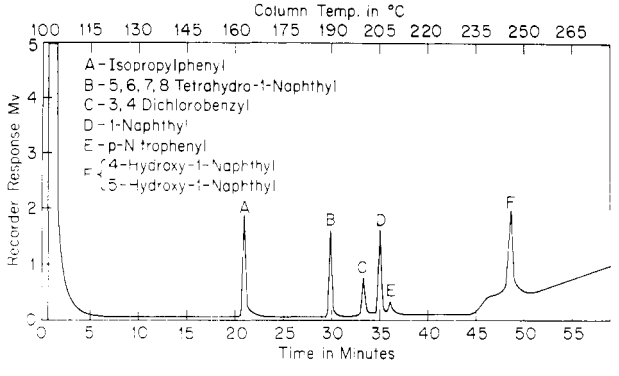

Figure 5. Chromatogram of *N*-methyl-*N*-acetyl carbamates on 1/2% Carbowax 20 M

Column.	8 ft., 5-mm. I.D.
Support.	Gas Chrom Q, 80- to 100-mesh
Flow rate, helium.	120 ml./min.
Injection port temp.	320° C.
Detector temp.	380° C.
Temp. program.	3° C./min.

broad peak is breakdown of unreacted carbaryl, and the third peak is *N*-acetyl carbaryl, showing both a radioactive and a mass peak. This illustrates the type of analytical results obtained for failure to obtain quantitative yield. The results of a quantitative yield of a mixture heated to 97° C. for 30 minutes are demonstrated by Figure 2. Only two radioactive peaks are found: the l-naphthyl acetate and the *N*-acetyl carbaryl. The reaction mixture was the same as the previous run with the exception of reaction conditions. When the reaction mixture from Figure 1 was allowed to stand for 24 hours, results identical with Figure 2 were obtained.

The chromatogram shown in Figure 3 is of an isothermal run at 200° C. of the reaction mixture from Figure 2. The first radioactive peak (solid line) is l-naphthyl acetate, while the second radioactive peak and the mass peak (dashed line) just preceding it are the *N*-acetyl carbaryl. No l-naphthol or other breakdown products could be determined and less than 1% l-naphthyl acetate was present.

Table II. Isothermal Retention Data[a] for Several *N*-Methyl-*N*-acetyl Carbamates on Three Columns

N-Methyl-*N*-acetyl Carbamates	5% SE-30[b] Temp., °C.	5% SE-30[b] Time, min.	2% SE-30[b] Temp., °C.	2% SE-30[b] Time, min.	0.5% 20 M[b] Temp., °C.	0.5% 20 M[b] Time, min.
Isopropylphenyl	200	3.3	150	6.7	165	5.8
p-Nitrophenyl	200	6.5	175	5.2	200	11.0
5,6,7,8-Tetrahydro-1-naphthyl	200	7.0	...	...	200	5.9
3,4-Dichlorobenzyl	200	8.2	175	7.0	200	7.2
1-Naphthyl	200	10.0	175	7.6	200	9.0
4-Hydroxy-1-naphthyl	220	13.5	200	10.8	230	5.2
5-Hydroxy-1-naphthyl	220	13.6	200	10.9		
1,4-Naphthyldi-	260	10.5	240	8.0		
1,5-Naphthyldi-	260	10.5	240	8.0		

[a] All data corrected for air peak.
[b] Eight feet long, 5-mm. I.D. columns, helium flow 120 ml. per minute, 80- to 100-mesh Gas Chrom Q, injection port temperature 320° C., detector temperature 380° C.

Table III. Retention Data at 200° C. for Carbowax 20 M Coated Open-Tube Column[a]

N-Methyl Carbamates	*N*-Derivatives	Time, Min.
Isopropylphenyl	Acetyl	1.4
5,6,7,8-Tetrahydro-1-naphthyl	Acetyl	5.0
p-Nitrophenyl	Methyl	5.4
1-Naphthyl	Methyl	6.2
3,4-Dichlorobenzyl	Acetyl	6.6
1-Naphthyl	Acetyl	8.6

[a] 150-foot copper column 1/8-inch I.D. with a film thickness of 0.2 micron, helium velocity 12.5 cm. per second, hydrogen flame detection, injection port temperature 320° C., and detector temperature 380° C.

Figure 4 is a temperature-programmed chromatogram of a mixture of *N*-acetyl-*N*-methyl carbamates prepared by adding 10 mg. of each carbamate to 2 ml. of acetic anhydride on the 5% SE-30 column at a flow rate of 120 ml. per minute. The initial temperature was 75° C. and the program rate 3° C. per minute. The injection temperature was 320° C. and the detector temperature 380° C. Fifty microliters of catalyst was used. The carbamates were added at 4° C. and the mixture was heated at 97° C. for 30 minutes. The absence of breakdown products and individual phenols or phenyl acetates indicates that acetylation was complete or of high yield. Experiments on the individual compounds confirmed these observations. The low response of the *p*-nitrophenyl (B) and the 3,4-dichlorobenzyl compounds (D) is detector response. The low response of the dicarbamates is due to the insolubility of the 1,5-naphthyldicarbamate in the acetylating reagent.

When the reaction mixture from the preceding system was chromatographed on a 0.5% 20 M packed column and programmed from 100° C. at 3° C. per minute, all other conditions remaining the same, the chromatogram in Figure 5 was obtained. The dicarbamates were not eluted because of the temperature limitations of the column. A small peak that sometimes appears prior to the 3,4-dichlorobenzyl derivative is the 2,3-dichloro isomer which was present in some samples and is not separated from the 3,4-isomer on SE-30. The loss of response of the *p*-nitrophenyl derivative has not as yet been determined, other than that it does not appear to be breakdown of the carbamate. A reaction mixture prepared as above and allowed to stand 24 hours gave an identical chromatogram on both SE-30 and 20 M columns.

Isothermal retention data on the 5% SE-30, 2% SE-30, and 0.5% Carbowax 20 M are given in Table II. The order of elution for each column is the same as the temperature-programmed determinations. Theoretical plate calculations for *N*-acetyl carbaryl for the three columns are: 5% SE-30, 3500; 2% SE-30, 3000; and 0.5% 20 M, 2500. The significant difference in the three columns other than elution temperature is the different order of elution of the *p*-nitrophenyl compound relative to *N*-acetyl carbaryl on the Carbowax and SE-30 columns. All three columns shown are stable under conditions described and are useful for detection and determination of carbamates as the *N*-acetyl derivatives.

In Table III are given the data at 200° C. obtained for an isothermal run on a 0.5 20 M open tube copper column 1/8 inch in outside diameter and 150 feet long. The average linear velocity of the air peak was 12.5 cm. per second. Both *N*-methyl and *N*-acetyl derivatives of the carbamates were used. The order of elution is the same as found for the packed systems. The effective efficiencies of the columns are slightly less than those of packed columns, and in general the only special advantage of such columns is the exceptionally low bleed which is obtained.

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