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## GAS CHROMATOGRAPHY OF N-METHYL AND N-ARYL CARBAMATES BY FLASH-HEATER REACTION WITH TRIMETHYLANILINIUM HYDROXIDE\*

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### SUMMARY

A simple derivatization procedure employing trimethylanilinium hydroxide (Methelute®) is described. This method may prove useful in the analysis of certain pesticidal carbamate residues. The flash-heater reaction product derived from N-aryl carbamates was identified as the N-methyl-N-aryl carbamate. For the N-methyl carbamates, however, a methyl substitution product (aryl methyl ether) was obtained rather than the anticipated N,N-dimethyl carbamate. Using propham and carbaryl as representative compounds for the two classes of carbamates, the degree of reaction for each with Methelute was estimated to be essentially quantitative. Chromatographic response was observed to be linear with increased concentration for the synthetic standards and the flash-heater products of propham and carbaryl. At the nanogram level, flash-heater reaction improved the sensitivity of detection of propham and carbaryl by approximately 30% and 400%, respectively.

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### INTRODUCTION

Pesticidal carbamate esters are generally grouped into two classes. The N-methyl carbamates are usually applied as insecticides and the N-aryl carbamates are used as herbicides. Because carbamates can decompose during gas-liquid chromatography (GLC), development of thermally stable derivatives for quantitative GLC analysis has been of considerable interest. Fishbein and Zielinski<sup>1</sup> have prepared thermally stable trimethylsilyl derivatives of some carbamates which can be chromatographed with the side chain intact. The elution time of the silyl derivative, however, was close to that of the parent carbamate in all cases studied. At the nanogram level, N-methyl carbamates have been detected by electron capture as their N-perfluoroacyl derivatives<sup>2,3</sup>. Perfluoroacylation may be too time consuming for im-

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plementation into rapid screening programs. Other approaches to GLC determination of N-methyl carbamates have been based on hydrolytic cleavage under basic or acidic conditions with subsequent derivatization of either the liberated phenol moieties<sup>4-8</sup> or methyl amine moiety<sup>9-13</sup>. The additional steps required have made these methods even less desirable, because much more time is consumed and the chance for pesticide loss is greatly increased. Moye<sup>14</sup> has described a method for on-column transesterification of an N-methyl carbamate to the alkyl-N-methyl carbamate with alcoholic sodium hydroxide. Conversion by this method is not quantitative; furthermore, this approach does not permit the analysis of the aryl moiety of the carbamate. The direct chromatography of N-methyl carbamates allowed rapid separation and identification of the intact carbamate<sup>15,16</sup>, but even with careful column selection some carbamate decomposition does occur.

Recently, a sodium hydride-methyl iodide N-alkylation reaction of N-aryl carbamates has been reported<sup>17</sup>. Alkylation, however, has proved useful only for the N-aryl carbamates, and sample preparation appears to be too time consuming for most rapid screening programs. Derivatization by flash-heater methylation with Methelute has recently been developed for the analysis of substituted phenylureas<sup>18</sup>. This methylation technique has provided a means for rapid qualitative and quantitative GLC analysis of phenylureas without side-chain decomposition. The carbamates, like the ureas, contain an active =NH group which may be derivatized by this same technique. Therefore, the flash-heater reaction of N-methyl and N-aryl carbamates with Methelute was investigated.

## EXPERIMENTAL

### Materials

Carbamate standards were obtained from commercial sources and were further purified by recrystallization from hexane-acetone. The N-aryl carbamates investigated were propham (isopropyl carbanilate), chlorpropham (isopropyl *m*-chlorocarbanilate), CEPC (2-chloroethyl *m*-chlorocarbanilate) (all from Pittsburgh Plate Glass, Pittsburgh, Pa., U.S.A.), and swep (methyl-(3,4-dichlorocarbanilate)) (Niagara Chemical Division, Middleport, N.Y., U.S.A.). The N-methyl carbamates studied were propoxur (*o*-isopropoxyphenyl methylcarbamate) (Chemagro, Kansas City, Mo., U.S.A.), dichlormate (3,4-dichlorobenzyl methylcarbamate) (Union Carbide, New York, N.Y., U.S.A.), carbofuran (2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate), and carbaryl (1-naphthyl methylcarbamate) (both from Niagara Chemical Division).

Trimethylanilinium hydroxide (Methelute<sup>®</sup>) was purchased as a 0.2 M methanolic solution from Pierce (Rockford, Ill., U.S.A.).

### Synthesis of authentic N-methyl propham and 1-methoxynaphthalene standards

N-Methylated propham (isopropyl-N-methylcarbanilate) was synthesized by a previously described sodium hydride-methyl iodide methylation procedure<sup>18</sup>. The product was purified by vacuum distillation. Boiling point (uncorrected) at 0.3 mm Hg was 84°; nuclear magnetic resonance (NMR) (CDCl<sub>3</sub>, tetramethylsilane internal reference); 1.20 (6H, doublet, -O-C(CH<sub>3</sub>)<sub>2</sub>H, *J* = 10Hz), 3.25 (3H, singlet, -N(CH<sub>3</sub>)-CO), 4.95 (1H, heptet, -O-CH(CH<sub>3</sub>)<sub>2</sub>, *J* = 10Hz), and 7.2 ppm (5H, singlet, mono-

substituted phenyl ring); mass spectrum,  $m/e$  193 (molecular ion) and  $m/e$  106 ( $M - C_4H_7O_2$ ).

An authentic sample of 1-methoxynaphthalene, the flash-heater reaction product of carbaryl, was prepared by the same procedure used for the synthesis of *N*-methyl propham. Reaction of carbaryl with sodium hydride and methyl iodide afforded a mixture containing 1-methoxynaphthalene and 1-naphthol. The 1-methoxynaphthalene was purified by preparative thin-layer chromatography (TLC). A solvent of benzene-hexane-acetone (3:6:2) was employed for the development of the silica gel HF plates. NMR ( $CDCl_3$ ): 3.80 (3H, singlet,  $-OCH_3$ ), 6.7–8.2 ppm (7H, multiplet, alpha-substituted naphthalene ring); mass spectrum,  $m/e$  158 (molecular ion).

#### Gas-liquid chromatography

A Barber-Colman 5000 chromatograph equipped with flame ionization detector, and glass columns (6 ft.  $\times$  5.0 mm I.D.) was used. The chromatographic columns were prepared according to the method described by Leibrand and Dunham<sup>19</sup>. Stationary phases (Table I) were coated on the solid support (Gas-Chrom Q, 80–100 mesh) by the slurry method. All columns were initially preconditioned from 60 to 225° using a temperature program rate of 1°/min, and the columns were then held at 225° for 18 h. Analyses were performed with the detector temperature (300°), inlet temperature (220°), hydrogen flow-rate (50 ml/min), air flow-rate (450 ml/min) and nitrogen carrier flow-rate (80 ml/min) held constant. All carbamates were chromatographed under isothermal conditions (Table I). Flash-heater reaction studies of propham and carbaryl with Methelute were performed on a 10% DC-LSX-3-0295 column.

TABLE I  
COLUMNS FOR GLC ANALYSIS OF FLASH-HEATER REACTED CARBAMATES

Column number	Column temperature (°C)		Stationary phase	$\Sigma \Delta I$ Values
	<i>N</i> -Methyl carbamates	<i>N</i> -Aryl carbamates		
1	—	160	10% SE-30 (methyl)	217
2	150	—	10% OV-101 (methyl)	229
3	155	160	8% OV-101	—
4	140	165	2% DC-LSX-3-0295 10% DC-LSX-3-0295 (trifluoropropyl, vinyl, methyl)	1557

The introduction of carbamate and Methelute into the gas chromatograph was performed by two previously described methods<sup>18,20</sup>. For rapid qualitative or semi-quantitative estimation, about 2  $\mu$ l of Methelute was first drawn into the syringe followed by the carbamate in 5  $\mu$ l of methanol. For quantitative measurements, the carbamate and Methelute were gently mixed in a small test tube before analysis.

#### Characterization of the flash-heater reaction products

To identify the products derived from flash-heater reaction of propham and carbaryl with Methelute, the products were trapped from the gas chromatograph in

capillary tubes. The isolated material in each case was then compared with authentic standards of N-methyl propham and 1-methoxynaphthalene by co-chromatography (TLC and GLC) and mass spectrometry to confirm their identity.

#### *Optimization of reaction with Methelute*

The molar ratio of Methelute to carbamate required for maximum detector response of the carbamates was determined using propham and carbaryl as representative compounds. Premixed samples containing 0.1 mmole of carbamate in 10 ml of methanol were prepared with Methelute to carbamate molar ratios ranging from 1:1 to 10:1. For each determination, 5  $\mu$ l (0.05  $\mu$ mole) of the carbamate-Methelute solution was injected into the gas chromatograph. The quantity of Methelute required for maximum carbamate reaction was estimated by the peak height method employing a standard curve prepared from authentic samples of N-methyl propham and 1-methoxynaphthalene.

#### *Linearity of response*

Standard methanolic solutions of N-methyl propham and 1-methoxynaphthalene, ranging in concentration from 1  $\mu$ g/5 ml to 8  $\mu$ g/5 ml, were prepared for determination of the linearity of response. The linearity of response with respect to flash-heater reaction was then estimated by using methanolic solutions of 2.0, 4.0, and 6.0  $\mu$ g/5 ml of propham and carbaryl with an approximate molar ratio of 10:1 of Methelute to carbamate.

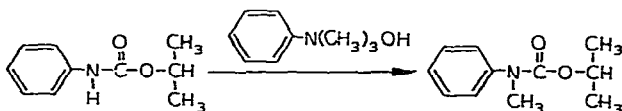
#### *Estimation of improvement in detector response*

Propham samples were prepared by adding 3.58 mg (0.02 mmole) of propham and 1 ml (0.2 mmole) of Methelute into a 100-ml volumetric flask and diluting to volume with methanol. Carbaryl (4.02 mg, 0.02 mmole) samples were prepared in an identical manner. For these analyses, 2  $\mu$ l (0.4 nmole) of carbamate solution was introduced into the gas chromatograph. These concentrations were selected because at this chemical level, a response of approximately 10% full scale deflection was observed for the underivatized carbamate. Measurements were taken with the electrometer attenuation setting at  $1 \times 8$ . Electronic noise at this attenuation setting afforded a 1% recorder deflection. The improvement in sensitivity of detection was determined by comparison of the peak heights obtained from flash-heater reacted propham and carbaryl with solutions of identical concentrations of propham and carbaryl.

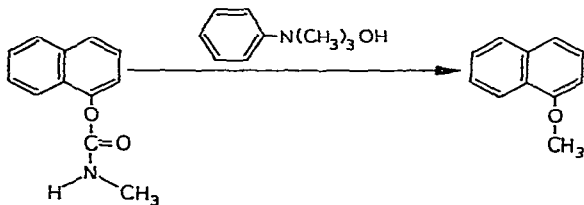
## RESULTS AND DISCUSSION

Upon GLC analysis of alkyl N-aryl carbamates, usually a portion of the carbamate thermally decomposed during chromatography. This loss of carbamate detection sensitivity could make quantitative analysis at the residue level unreliable. Derivatization with Methelute, however, allowed chromatography of N-aryl carbamates without decomposition. The flash-heater reaction was very reproducible and essentially quantitative at the nanogram level provided the carbamate had only one position available for reaction. An attempt was made to methylate phenmedipham (methyl *m*-hydroxycarbanilate *m*-methylcarbanilate) (supplied by NOR-AM Agricultural Products, Woodstock, Ill., U.S.A.) with Methelute; however, numerous

peaks appeared upon chromatography. The multiple peaks apparently resulted from incomplete reaction of Methelute with phenmedipham. Similar results were also obtained in the flash-heater methylation of monomethylmonuron<sup>18</sup>. Since monomethylmonuron and phenmedipham both contain more than one position available for methylation, several products can be realized by incomplete reaction with Methelute. Therefore, it appears that this derivatization technique is only useful for compounds that contain one available group for methylation. The reaction given below illustrates flash-heater methylation of an N-aryl carbamate (propham) to yield a thermally stable N-methyl analog.



Flash-heater reaction of the aryl N-methyl carbamates with Methelute did not yield an aryl N,N-dimethyl carbamate; rather, a methyl ether of the aryl moiety was obtained. Flash-heater reaction with Methelute could provide a method for the quantitative GLC determination for aryl N-methyl carbamates, provided the alcohol of the aryl or heterocyclic moiety was not present in nature. The reaction given below shows the flash-heater reaction of a N-methyl carbamate (carbaryl) with Methelute to obtain the aryl methyl ether.



The product from the reaction of propham with sodium hydride and methyl iodide was characterized as the N-methyl analog of propham by NMR and mass spectrometry. The identity of the flash-heater methylated product derived from propham was verified by trapping the material from the gas chromatograph and comparing it with standard N-methyl propham. Both materials were identical in all respects upon examination by GLC co-chromatography and mass spectrometry. Employing the same synthetic procedure with carbaryl, an aryl methyl ether was obtained. This ether was characterized as 1-methoxynaphthalene by NMR and mass spectroscopy. The product from flash-heater reacted carbaryl with Methelute was trapped from the gas chromatograph and compared with authentic 1-methoxynaphthalene. Mass spectrometry and co-chromatography (GLC, TLC) verified the identity of this flash-heater product as 1-methoxynaphthalene.

Because N-methyl carbaryl was not obtained from flash-heater reaction of carbaryl with Methelute, another N-methyl carbamate (carbofuran) was reacted with Methelute by this technique to determine whether methyl substitution was a general reaction for N-methyl carbamates. Comparison of the mass spectra of flash-heater reacted carbofuran with an authentic sample of 2,3-dihydro-2,2-dimethyl-7-methoxybenzofuran showed identical molecular ions ( $m/e$  178) and the same fragmentation

TABLE II

RETENTION VALUES OF THE PRODUCTS DERIVED FROM THE FLASH-HEATER REACTION OF N-METHYL AND N-ARYL CARBAMATES WITH METHELUTE

Compound	$t_R$ (min)			
	Column 1	Column 2	Column 3	Column 4
<i>N-methyl carbamates</i>				
Propoxur	—	4.1	2.9	3.4
Carbofuran	—	6.9	5.4	5.9
Dichlormate	—	8.3	6.3	6.9
Carbaryl	—	11.9	9.2	11.6
<i>N-aryl carbamates</i>				
Propham	5.1	—	5.9	4.2
Chlorpropham	10.8	—	11.7	7.1
CEPC	9.9	—	10.6	8.3
Sweep	18.0	—	20.0	16.5

pattern. Therefore, it appears that N-methyl carbamates will generally afford the methyl aryl ether by flash-heater reaction with methelute.

Retention times ( $t_R$ ) for the separation of the flash-heater methylated products of N-aryl carbamates and the flash-heater reaction products of N-methyl carbamates with different chromatographic columns are given in Table II. An indication of polarity effects on the stationary phases may be estimated by utilization of the McReynolds constants<sup>21</sup>. The numerical value  $\Sigma\Delta I$  (Table I)<sup>22</sup> assigned to each phase was derived from the summation of the McReynolds  $\Delta I$  values obtained for benzene, 1-

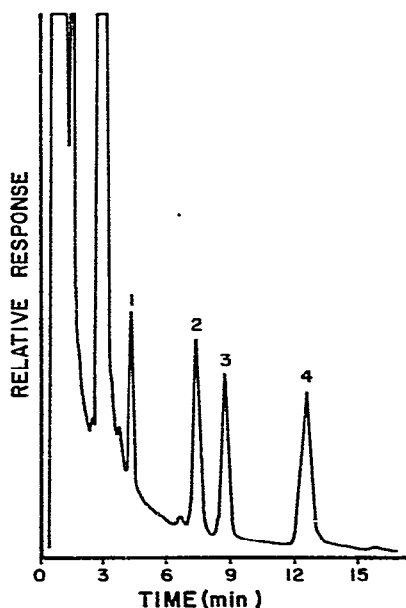


Fig. 1. Separation of a mixture of the flash-heater reacted products of N-methyl carbamates using a 10% OV-101 column. 1, Propoxur; 2, carbofuran; 3, dichlormate; 4, carbaryl.

butanol, 2-pentanol, nitropropane and pyridine. As a general guide to selectivity, higher  $\Sigma AI$  values normally indicate an increase in polarity of the stationary phase.

A 10% OV-101 ( $\Sigma AI$  229) column achieved the best separation for the flash-heater reacted products of N-methyl carbamates (Fig. 1). However, all columns (Table II) tested gave acceptable resolution. The very large peak observed in Fig. 1 just before the elution of flash-heater reacted propoxur was caused by the methylation reagent. On the other hand, Methelute eluted essentially with the solvent during chromatography of the derivatized N-aryl carbamates (Fig. 2) because a higher temperature was employed for that class of compounds.

A 10% DC-LSX-3-0295 ( $\Sigma AI$  1557) column provided the best results of all the columns (Table II) utilized for the separation of the N-aryl carbamate derivatives.

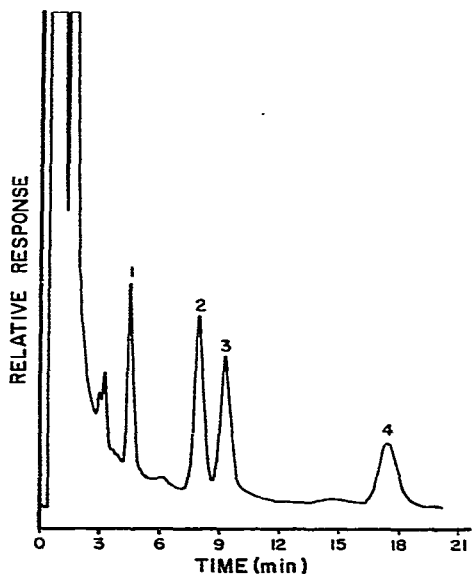


Fig. 2. Separation of a mixture of flash-heater methylated N-aryl carbamates using a 10% DC-LSX-3-0295 column. 1, Propham; 2, chlorpropham; 3, CEPC; 4, swep.

The separation achieved by the 10% DC-LSX-3-0295 column is shown in Fig. 2. Although a 10% OV-225 column gave better separation of the N-aryl carbamate derivatives, extraneous peaks appeared during chromatography. These peaks were probably caused by carbamate decomposition during chromatography because a higher column temperature was required for elution on the more polar column. Employing a non-polar column of 10% SE-30 ( $\Sigma AI$  217) or a mixed column of 8% OV-101 and 2% DC-LSX-3-0295, CEPC was eluted earlier than chlorpropham (Table II). When the polar 10% DC-LSX-3-0295 column was employed, however, the reverse situation occurred.

By varying the molar ratios of Methelute to carbamate, the quantity of Methelute required for maximum reaction of propham and carbaryl was estimated. An approximate molar ratio of 2:1 of Methelute to carbamate ensured maximum reaction of the representative compounds. Reaction of carbaryl with Methelute was

estimated at approximately 99%. On the other hand, derivatization of propham was estimated at 98%. After the elution of methylated propham, a very small propham peak was observed.

Propham and carbaryl samples were also injected into the gas chromatograph without mixing the carbamate and Methelute before analysis. To ensure maximum reaction of the carbamates with Methelute a molar ratio of approximately 15:1 of Methelute to carbamate was used. Results by this method of sample introduction showed a consistent 85% response to the introduced material. Therefore, sample introduction without premixing carbamate and Methelute appears useful only for rapid qualitative and semi-quantitative analysis.

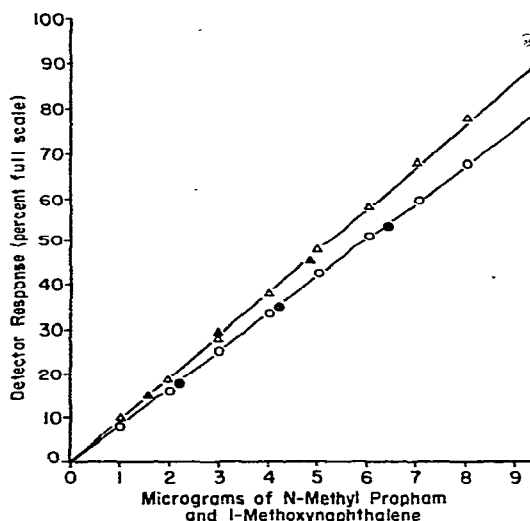


Fig. 3. Linearity of response with increased concentration of the flash-heater reaction products of propham and carbaryl. ○, N-methyl propham; ●, propham + Methelute (1:10); △, 1-methoxynaphthalene; ▲, carbaryl + Methelute (1:10).

Fig. 3 shows the detector response curves of N-methyl propham and 1-methoxynaphthalene prepared from authentic standards. The chromatographic response for the two compounds was observed to be linear with increased concentration. The curves also passed through zero, indicating that no measurable degradation was taking place on the column. The flash-heater reaction method was then tested to determine whether a linear response would also be obtained with increased concentration. The results, as shown in Fig. 3 by the solid blocks, clearly indicate a linear response with respect to concentration.

Pesticide residue analyses are generally performed at very low chemical levels. Therefore, any method that could improve the sensitivity of detection of carbamates would be considered valuable. To simulate residue levels, nanogram concentrations of propham and carbaryl were used. At these concentrations, a 10% recorder deflection was obtained. Response of the flash-heater reacted products of propham and carbaryl were then compared with the response for identical concentrations of propham and carbaryl. The flash-heater reaction technique improved the detector re-



sponse of propham and carbaryl at the residue level by approximately 30% and 400%, respectively. The marked increase in detector response for the flash-heater reacted product of carbaryl could be anticipated because N-methyl carbamates are more thermally labile than N-aryl carbamates. Another factor that may contribute to the improvement in detection is the shorter retention time for the flash-heater reacted product in comparison with the parent compound. A shorter residence time on-column reduces peak spreading; thus, an improvement in detector response is obtained.

Flash-heater reaction with Methelute is a rapid method for detection of certain N-methyl and N-aryl carbamate pesticides. The technique is reproducible, essentially quantitative, and more sensitive in response at the nanogram level. Therefore, this method appears to have value if implemented into screening programs for carbamate pesticides at the residue level.

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