

## Notes

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### Gas chromatography of halogenated carbamates

#### II. N-Trichloroacetyl derivatives

The gas chromatographic analysis of N-chloroethyl and N,N-bis-(2-chloroethyl) carbamates has been reported earlier. References to the analysis of nitrogen mustard derivatives and chlorinated carbamates were cited in that paper<sup>1</sup>. The preparation of halogen-containing substituted urethanes via reaction of halogen-substituted fatty acid acyl chlorides with compounds of type RNHCOOR' has been reported<sup>2</sup>. Other derivatives containing the trichloroacetyl moiety have been prepared by the reaction of trichloroacetyl chloride with amino acids<sup>3</sup> and aromatic amino acids<sup>4</sup>. Trichloroacetanilides were made by condensation of aromatic amines with trichloroacetic acid<sup>5</sup>.

The preparation of N-trichloroacetyl alkyl and halogenated aryl carbamates has afforded the opportunity of investigating the thermal stability of an N-acyl carbamoyl grouping during gas chromatographic assay. A secondary result of this study was the elaboration of the relative electron capturing capability of trichloroacetamide *vs.* the appropriate halogenated phenol or alcohol formed by the thermal rupture of the highly labile precursor carbamates during chromatography.

#### *Experimental*

The N-trichloroacetyl carbamates were prepared via reaction of trichloroacetyl isocyanate\* with the respective alkyl, aryl, and cyclic alcohols and halogenated phenols, and recrystallized from hexane. Melting points were determined on a Fisher-Johns melting point apparatus.

Gas chromatography was carried out on acetone solutions, both with an electron capture detector (Aerograph Hy-FI Model 600-B containing a column of 5 ft. by 0.125 in. O.D. Teflon tubing packed with 2% neoglycol succinate (NGS) and 1% polyvinylpyrrolidine (PVP) on 80-100 mesh acid-washed Chromosorb P) and with a flame ionization detector (F & M Model 1609 containing a column of 6 ft. by 0.25 in. O.D. glass coil packed with 4% QF-1 fluorosilicone on 80-100 mesh HMDS-pretreated Chromosorb W). Specific analytical operating conditions are given in the footnotes to Table I.

#### *Results and discussion*

The analytical results for the N-trichloroacetyl chlorophenyl and trihaloethyl carbamates are given in Table I.

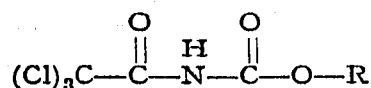
The 2,2,2-trifluoroethyl derivative appeared as a single peak under the conditions employed for the QF-1 column, without degradation to trichloroacetamide

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\* Obtained from Eastman-Kodak, Rochester, N.Y., U.S.A.

TABLE I

GAS CHROMATOGRAPHY OF N-TRICHLOROACETYL CARBAMATES



R	m.p. (°C)	Relative retention <sup>a</sup>		Relative sensitivity <sup>b</sup>		
		E.C. <sup>c</sup>	F.I. <sup>d</sup>	E.C.	F.I.	F.I./E.C. ratio
		<i>Alcohol</i>	<i>Alcohol</i>	<i>Alcohol</i>	<i>Alcohol</i>	
2,2,2-Trifluoroethyl	95-97	e	e	e	e	—
2,2,2-Trichloroethyl <sup>f</sup>	101-102	0.067	0.072	7.5	2.6 <sup>h</sup>	0.35
2,2,2-Tribromoethyl	124-125	0.34	0.33	3.4	4.1	0.83
		<i>Phenol</i>	<i>Phenol</i>	<i>Phenol</i>	<i>Phenol</i>	
<i>o</i> -Chlorophenyl	94-95	0.22	0.19	0.14	9.7 <sup>h</sup>	69
<i>m</i> -Chlorophenyl	92-93	0.52	0.58	0.089	10.8	121
<i>p</i> -Chlorophenyl	105-106	0.58	0.62	0.14	30.1	215
2,3-Dichlorophenyl	84-85	0.91	0.50	2.4 <sup>h</sup>	33.7	14
2,4-Dichlorophenyl	49-51	0.79	0.48	2.1 <sup>h</sup>	5.7	2.7
2,5-Dichlorophenyl	95-97	0.88	0.48	1.2 <sup>h</sup>	7.5	6.2
2,6-Dichlorophenyl	81-83	0.50	0.66	1.4 <sup>h</sup>	4.0	2.9
3,4-Dichlorophenyl	55-57	h	1.8	1	23.1	—
3,5-Dichlorophenyl	123-125	0.80 <sup>l</sup>	1.4	1	20.4	—
2,4,5-Trichlorophenyl	55-57	4.3	1.2	27.5	5.2	0.19
2,4,6-Trichlorophenyl	98-100	1.3	1.3	22.7	7.4	0.33
2,3,4,6-Tetrachlorophenyl	58-60	10.8	3.3	35.9	3.5	0.098
Pentachlorophenyl	122-123	k	7.3 <sup>m</sup>	k	1.1 <sup>m</sup>	—

<sup>a</sup> Relative to trichloroacetamide as 1.00. Trichloroacetamide eluted at 3.4 minutes on QF-1 (flame detector) and at 5.3 minutes on NGS-PVP (E.C. detector).

<sup>b</sup> Relative to trichloroacetamide as 1.0. Sensitivity of trichloroacetamide was approximately 3.8 mm<sup>2</sup>/μg on flame ionization and 2.740 mm<sup>2</sup>/μg on electron capture.

<sup>c</sup> Electron capture detector. Column: 2% NGS and 1% PVP on 80-100 mesh acid-washed Chromosorb P, 5 ft. by 0.125 in. O.D. Teflon column. Conditions: column 160°; injector 65 V; detector 160°; 10 input impedance; 1 × output sensitivity; nitrogen carrier 60 ml/min; 250 milluries tritium.

<sup>d</sup> Flame ionization detector. Column: 4% QF-1 on 80-100 mesh HMDS-pretreated Chromosorb W, 5 ft. by 0.25 in. O.D. glass coil column. Conditions: column 110°; injector 70 V; range 1000; air 300 ml/min; hydrogen 75 ml/min; nitrogen carrier 86 ml/min.

<sup>e</sup> Intact carbamate had a relative retention of 3.6 on QF-1. Trifluoroethanol eluted at the solvent front and could not be assigned a  $t_R$  value for either column or a sensitivity value on NGS-PVP. The relative sensitivity of standard 2,2,2-trifluoroethanol was 1.6 on QF-1.

<sup>f</sup> Trichloroacetamide peak did not appear with the flame ionization system.

<sup>g</sup> Determined by separate chromatography of trichloroacetamide, chlorophenol and trihaloethanol standards.

<sup>h</sup> Only trichloroacetamide peak was obtained.

<sup>i</sup> 3,4- and 3,5-dichlorophenols did not produce peaks under the conditions employed.

<sup>j</sup> Appeared on analysis of the carbamate. See footnote i.

<sup>k</sup> Absence of pentachlorophenol peak.

<sup>m</sup> Relative retention changes to 5.1 at a column temperature of 160° and a carrier flow of 70 ml/min, with a concomitant change in relative sensitivity to 1.6.

and 2,2,2-trifluoroethanol. The tribromo and trichloro derivatives on the other hand, underwent rupture with the release of the amide and the respective trihaloethanol. All of the chlorophenyl derivatives evidenced cleavage to trichloroacetamide and the respective chlorophenol. The retention data indicate the expected trend of increased

retention with increased molecular weight for the chlorophenols. Separations appeared best on the NGS-PVP column. Comparison of the results obtained on this column with those of the QF-1 column indicates that mono-, di-, and tri-chlorophenols are more readily resolved on polar substrates.

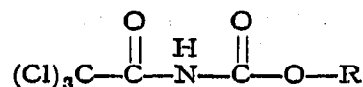
In the instances where cleavage to 2,2,2-trichloroacetamide and the chlorinated alcohol or phenol occurred, no third peak for residual intact carbamate was noted. If it is assumed that cleavage to the amide and phenol (or alcohol) components is stoichiometrically 1:1, one may calculate the sensitivity of the phenols and alcohols relative to trichloroacetamide via the respective chromatogram peak areas. The electron-capturing capacities thus obtained for the chlorophenols were in the order of tetra > tri > di > mono; and in general, trichlorophenols > trihaloethanols > dichlorophenols.

The relative sensitivities observed with the flame ionization detector were roughly mono-, dichlorophenols > trichlorophenols > trihaloethanols > tetrachlorophenol > pentachlorophenol. These latter results suggest a general decline in sensitivity as the halogen content of the molecule increases. It is of interest that considerable variation in relative sensitivity exists among the dichlorophenol isomers, the higher sensitivities being associated with a chlorine atom attached in the 3 position. It is questionable, however, whether this alone is the governing factor for sensitivity, since the 5 position is also *meta* to the hydroxy group and the 2,5-isomer does not evidence such a level of sensitivity.

It has been stated by other investigators<sup>6</sup> that a flame/EC response ratio could

TABLE II

MELTING POINT DATA OF MISCELLANEOUS ALKYL, ACYLIC AND ARYL N-TRICHLOROACETYL CARBAMATES



<i>R</i>	<i>Mol. wt.</i>	<i>M.p.</i> (°C)
Methyl	220	100-101
Ethyl	234	57-58
2-Propynyl	244	54-55
Allyl	246	32-33
<i>n</i> -Propyl	248	44-45
Isopropyl	248	73-74
<i>n</i> -Butyl	262	38-39
<i>sec.</i> -Butyl	262	61-63
Isobutyl	262	80-81
<i>tert.</i> -Butyl	262	99-100
2-Chloroethyl	269	62-63
Cyclopentyl	274	65-66
Phenyl	282	108-109
Cyclohexyl	288	89-90
Benzyl	296	83-85
Heptyl	304	28-29
Phenethyl	310	43-44
2-Bromoethyl	313	54-55
Piperonyl	340	88-89

be taken as a characteristic value of a particular electron-capturing molecule. This ratio is given in the last column of Table I and shows the general trend: monochlorophenols  $\gg$  dichlorophenols  $>$  trihaloethanols  $>$  trichlorophenols  $>$  tetrachlorophenol.

A variety of N-trichloroacetyl alkyl carbamates, including the cyclic pentyl and hexyl, and the aromatic phenyl, benzyl, phenethyl, and piperonyl derivatives, were synthesized and analyzed. Only the 2,2,2-trichloroacetamide peak appeared on the recorder chart for each of these compounds using either detector system. The absence of the alcohol component for the electron-capture system was due to lack of component sensitivity, and for the flame ionization system to rapid elution of the alcohol component which in most cases was lost in the solvent peak under the analytical conditions employed. The melting points of these derivatives are reported in Table II.

Concerning the lability of the N-trichloroacetyl carbamates to gas chromatographic analysis, it is felt that alternate analytical conditions such as column temperature considerations could influence the stability of these derivatives. Stability, to be sure, has been observed during thin-layer chromatography<sup>7</sup>. The relationship of thermal rupture to analytical temperature is presently under investigation.

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