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ANALYSIS OF SULPHUR-CONTAINING CARBAMATES BY FORMATION OF DERIVATIVES IN THE GAS–LIQUID CHROMATOGRAPH USING TRIMETHYLPHENYLAMMONIUM HYDROXIDE

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SUMMARY

Carbamates injected into the gas–liquid chromatograph with trimethylphenylammonium hydroxide react to give derivatives with good gas–liquid chromatographic properties. Oximecarbamates yield methoximes by this procedure, and substituted-phenyl N-methylcarbamates yield anisoles. Yields over a range of conditions were generally better than 90%, except from aldoximecarbamates where competing reactions intervened. Although only sulphur-containing carbamates were studied, it should be possible to extend the reaction to other carbamates.

INTRODUCTION

Carbamate pesticides present difficult analytical problems due to their instability and low volatility in gas–liquid chromatography (GLC) columns. Recent approaches to these problems have been reviewed by Ruzicka[1], Thornburg[2] and Dorough and Thorstenson[3]. Cochrane[4] has reviewed the preparation of derivatives from carbamates for estimation by GLC or fluorimetry.

Direct GLC of methomyl[5], an oximecarbamate, and of several other carbamates including substituted-phenyl N-methylcarbamates[6–8] has been reported, but exacting chromatographic conditions are required to prevent decomposition. Aldicarb, an aldoxime-N-methylcarbamate, and its oxidation product, aldicarb sulphone, may be assayed as their corresponding nitriles produced by thermal degradation in the heated injection ports of GLC systems[9]. The hydrolysis products of carbamates also have been subjected to GLC directly: examples include the oxime from methomyl[10] and the phenols from methiocarb and its oxidation products[11]. Moye[12] has reported a novel procedure involving injection of N-methylcarbamates with methanol containing a little aqueous sodium hydroxide solution, whence transesterification occurs yielding methyl N-methylcarbamate.

Alkylation of compounds with –NH groups yields derivatives with improved stability and GLC characteristics. Methylated derivatives of several classes of such compounds including carbamates have been prepared by base-catalysed reaction

with methyl iodide[13]. The potentially simpler procedure of on-column methylation using trimethylphenylammonium hydroxide (TMAH) has been applied to barbiturates[14,15], cannabis metabolites[16], diphenylhydantoins[17,18], fatty acids[19], and phenylurea herbicides[20]. We have found that injection of the oximecarbamate oxamyl with TMAH results in loss of the carbamate group with formation of the corresponding methoxime in high yield, this derivative also having good GLC properties. This paper reports on the applicability of this technique to the GLC analysis of a series of sulphur-containing oximecarbamate and substituted-phenyl N-methylcarbamate insecticides and nematocides.

EXPERIMENTAL

Materials and reagents

The nitriles, some oximes and phenols and the carbamates were analytical grade supplied by the respective manufacturers; the other oximes and phenols were prepared by hydrolysis of the corresponding carbamates with 1 N aqueous sodium hydroxide. Stock solutions of test substances (approximately 1 mg/ml) were prepared in analytical-grade acetone or ethyl acetate and stored at $-16°$; diluted solutions were prepared immediately prior to use. TMAH was purchased as a 0.1 M solution in methanol from Eastman-Kodak (Rochester, N.Y., U.S.A.). Thin-layer chromatography (TLC) was carried out on pre-coated plates (0.25 mm thick silica gel 60 F_{254}, Merck, Darmstadt, G.F.R.) used as received.

Preparation of derivatives

Preparation of oxamyl methoxime. Oxamyl (I) (1.0 g) was dissolved in 10 ml ethanol and 50 ml 1 N aqueous sodium hydroxide was added. After leaving this solution for 2 h at room temperature to ensure complete hydrolysis of oxamyl to its oxime, 2.0 ml dimethyl sulphate were added and the mixture stirred for a further 2 h. The product was extracted with dichloromethane (2 × 50 ml) and the pooled extracts, dried over anhydrous sodium sulphate, were rotary evaporated to a pale yellow oil. This material was purified by chromatography on a 100 mm × 30 mm I.D. silica gel column using diethyl ether–acetone mixtures as eluent to give oxamyl methoxime (II) (287 mg, 36%) as a colourless oil. Nuclear magnetic resona nce (NMR) (CDCl₃): $\tau = 6.02$ (–OCH₃); $\tau = 6.91, 6.94$ [(CH₃)₂N–]; $\tau = 7.73$ (–SCH₃).

The methoximes and anisoles (substituted-phenyl methyl ethers) listed in Table I were prepared similarly from their respective carbamates, with the exception of the anisoles from methiocarb sulphoxide and methiocarb sulphone which were prepared by dilute peracetic acid oxidation of methiocarb anisole. The structures of these derivatives were confirmed by NMR. The methoxime of DS-15647 could not be satisfactorily prepared by the above methylation procedure and was not available for this study. Table I gives the TLC properties of the carbamates and their derivatives together with the chemical structures of the carbamates. The compounds were located on the TLC plates by quenching of the fluorescent indicator in the silica gel at 254 nm, or by spraying the plates with 0.5% 2,6-dibromo-p-benzoquinone-4-chlorimine in cyclohexane followed by heating to 110° for 1 5 min when the compounds appeared as brown spots on a pale backgro und.

TABLE I

STRUCTURES AND TLC PROPERTIES OF CARBAMATES AND DERIVATIVES

Solvent systems: (A) hexane–acetone (2:1); (B) diethyl ether–acetone (4:1).

Compound	Structure	R_F value					
		Carbamates		Corresponding phenol or oxime		Corresponding methoxime or anisole	
		A	B	A	B	A	B
Oxamyl (DuPont 1410)	$(CH_3)_2\,NC(=O)(CH_3S)C=NOC(=O)NHCH_3$	0.094	0.20	0.13	0.37	0.31	0.44
Methomyl	$CH_3(CH_3S)C=NOC(=O)NHCH_3$	0.19	0.35	0.29	0.54	0.51	0.62
DuPont 1642	$CH_3(CH_3S)C=NOC(=O)NH_2$	0.11	0.28	0.29	0.54	0.51	0.62
DS-15647 (thiofanox)	$(CH_3)_3C,\ CH_3SCH_2 / C=NOC(=O)NHCH_3$	0.40	0.59	0.53	0.75	—*	—*
DS-15647 sulphoxide**	—	0.09	0.11	—*	—*	—*	—*
DS-15647 sulphone**	—	0.23	0.37	—*	—*	—*	—*
Aldicarb	$CH_3S-C(CH_3)(CH_3)-CH=NOC(=O)NHCH_3$	0.35	0.53	0.50	0.71	0.69	0.76
Aldicarb sulphoxide	—	0.03	0.07	0.07	0:16	0.19	0.25
Aldicarb sulphone	—	0.11	0.23	0.24	0.55	0.42	0.60
Tirpate	$CH_3-S/S-C(CH_3)-CH=NOC(=O)NHCH_3$	0.34	0.53	0.48	0.67	0.63	0.70
Methiocarb	$CH_3S-C_6H_2(CH_3)(CH_3)-OC(=O)NHCH_3$	0.47	0.69	0.50	0.73	0.65	0.77
Methiocarb sulphoxide	—	0.08	0.16	0.08	0.18	0.17	0.24
Methiocarb sulphone	—	0.21	0.49	0.24	0.56	0.39	0.62

* Compounds were not available for this study.

** The sulphide –SCH$_3$ is replaced by –SOCH$_3$ and –SO$_2$CH$_3$ in the sulphoxide and sulphone analogues, respectively.

Gas–liquid chromatography

Apparatus. The gas chromatograph used was a Pye 104 series oven fitted with a venting valve[21] and a United Analysts flame photometric detector operated in the sulphur mode (394-nm filter) according to the manufacturer's instructions. 0.9 m ×

3 mm O.D. stainless-steel columns were employed, packed with 80–100 mesh Chromosorb W coated with 0.5% Carbowax 20M + 5% SE-30 or with 5% QF-1. The nitrogen carrier gas flow-rate was maintained at 60 ml/min in the isothermal studies. The glass injection port, 90 mm × 3 mm I.D., was lightly packed with non-silanised glass wool and maintained at 210° (except where otherwise stated).
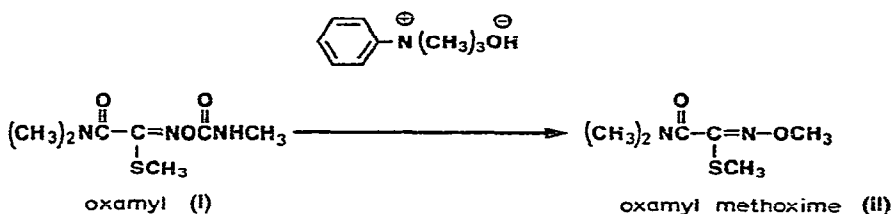
Injection procedure. Chemicals were usually taken into a 10-μl syringe in the following order: solvent (0.2 μl), sample solution (2.0 μl) and, finally, 0.1 M TMAH in methanol (0.5 μl). (The initial 0.2 μl of solvent may be omitted if so desired to simplify the injection procedure). Preformed derivatives were injected in the same volume of solvent (2.7 μl) without TMAH. The column effluent was vented to the atmosphere for 30–60 sec after injection.

Identification of the derivatives. The derivative formed by injection of oxamyl with TMAH was trapped in a cooled glass capillary from the column effluent. It was shown to be identical with authentic oxamyl methoxime (II) by co-chromatography on GLC and TLC, and by NMR. Derivatives formed similarly from other carbamates had the same GLC retention times as the corresponding methoximes or anisoles where these were available by independent synthesis.

Estimation of the yield of the derivatives. Yields of derivatives obtained from injection of carbamates (about 20 ng) with TMAH were estimated from the peak heights by interpolation from log–log calibration curves constructed for each of the authentic derivatives.

RESULTS AND DISCUSSION

Carbamates react with TMAH in the gas chromatograph to give derivatives with improved GLC stability and volatility. Phenyl N-methylcarbamates yield anisole derivatives by this procedure, and oximecarbamates yield methoximes, as illustrated by the reaction of oxamyl (I):

$$\langle \bigcirc \rangle - \overset{\oplus}{N}(CH_3)_3 \overset{\ominus}{OH}$$

$$(CH_3)_2 N\overset{\overset{O}{\|}}{C} - \underset{\underset{SCH_3}{|}}{C} = NO\overset{\overset{O}{\|}}{C}NHCH_3 \longrightarrow (CH_3)_2 N\overset{\overset{O}{\|}}{C} - \underset{\underset{SCH_3}{|}}{C} = N - OCH_3$$

oxamyl (I)   oxamyl methoxime (II)

The derivative formed thus from oxamyl was shown to be identical to independently synthesised oxamyl methoxime by GLC, TLC and NMR.

The yield of derivative from oxamyl (23 ng) injected with TMAH was examined using a range of conditions, and found to be unaffected by: varying the injection port temperature from 180°–300°; varying the volume of TMAH solution from 0.2–0.7 μl; reversing the order of the TMAH and the sample solution in the syringe. Thus, use of the procedure is straightforward and gives consistent results over a wide range of conditions.

Yields and GLC retention times of derivatives formed by this procedure from

TABLE II

YIELDS AND RETENTION TIMES OF THE DERIVATIVES FORMED BY THE ON-COLUMN REACTION OF TMAH WITH SOME CARBAMATES

Column, 0.5% Carbowax 20M + 5% SE-30.

Compound	Column temperature (°C)	Retention time (min)	Yield (%)
DuPont 1642	80	2.5	99
Methomyl	80	2.5	93
DS-15647	110	2.0	— *
DS-15647 sulphoxide	150	2.35	—
DS-15647 sulphone	150	2.60	—
Oxamyl	150	2.60	97
Methiocarb	150	3.6	90
Methiocarb sulphoxide	200	3.6	97
Methiocarb sulphone	200	3.9	100

* Yields were not measured for DS-15647 and its oxidation products as the authentic methoximes were not available.

some oximecarbamates (other than those from aldoximes) and substituted-phenyl N-methylcarbamates are given in Table II. The measured yields (for six compounds) were 90% or higher. Single peaks were obtained from each compound.

Yields of methoximes resulting from injection of aldoximecarbamates with TMAH varied from 0–91% (Table III), one cause being the competing thermal degradation of aldoximecarbamates to the corresponding nitriles[9]. Thus the fate of aldicarb by this procedure could be accounted for entirely by methoxime and nitrile formation (91% and 9%, respectively). However, Tirpate yielded only 38% methoxime, together with a smaller amount of another material presumed to be the nitrile. As there is also a 60–70% loss of preformed Tirpate methoxime on co-injection with

TABLE III

YIELDS AND RETENTION TIMES OF THE METHOXIME DERIVATIVES AND NITRILES FORMED BY THE ON-COLUMN REACTION OF TMAH WITH SOME ALDOXIMECARBAMATES

Column, 0.5% Carbowax 20M + 5% SE-30.

Compound	Column temperature (°C)	Methoxime		Nitrile	
		Retention time (min)	Yield (%)	Retention time (min)	Yield (%)
Aldicarb	80	2.3	91	1.45	9
Tirpate	130	3.4	38	2.7*	— **
Aldicarb sulphoxide	130	2.9	0	2.1*	— **
Aldicarb sulphone	150	1.5	0	1.25	8

* Retention time of the peak produced by injection of the carbamate alone and presumed to be the corresponding nitrile formed by thermal degradation. The more extensive degradation product methacrylonitrile has been reported previously to be formed during GLC of aldicarb sulphoxide[9], but this would not have been detected in our GLC system.

** The yields were small but could not be measured accurately in the absence of the authentic nitriles.

TMAH, it is likely that the methoxime is formed in high yield and subsequently partially decomposed to apparently involatile products, no other GLC peaks being observed.

Aldicarb sulphoxide and aldicarb sulphone injected with TMAH gave only low yields of the corresponding nitriles and no detectable amounts of the methoximes. In an attempt to elucidate the reactions occurring, some possible products from aldicarb sulphone were themselves injected with TMAH: aldicarb sulphone methoxime was largely decomposed, the only other peak observed representing variable but small amounts of the nitrile; aldicarb sulphone nitrile was about 90% decomposed, no other peaks being observed; aldicarb sulphone oxime yielded no peaks at all. This last observation suggests that the methoxime is not formed at all under these conditions (see below), but the alternative explanation, *viz.* that the methoxime is formed and then degraded perhaps via the nitrile, cannot be entirely ruled out. No attempt was made to increase yield of the methoxime derivatives by varying the GLC conditions or reaction procedure, because the aldoximecarbamates can be assayed adequately by thermal degradation in the gas chromatograph to the corresponding nitriles[9].

Fig. 1 shows the separation of carbamates in mixtures injected with TMAH using temperature programming. Because of the wide range of volatility of the derivatives, the carbamates were for convenience divided into two groups based upon their GLC retention times. Sulphoxides were not included as they were inadequately resolved from the corresponding sulphones, and in analytical procedures are likely to be oxidised to the sulphones prior to GLC estimation. The methoximes from oxamyl and DS-15647 sulphone were not resolved on the 0.5% Carbowax 20M + 5% SE-30 column, but could be separated on the 5% QF-1 column (retention times 2.75 and 2.28 min, respectively, at 180°).

The reaction of carbamates with TMAH appears to proceed in two steps: initial loss of the carbamate group to give the hydroxy moiety (oxime or phenol),
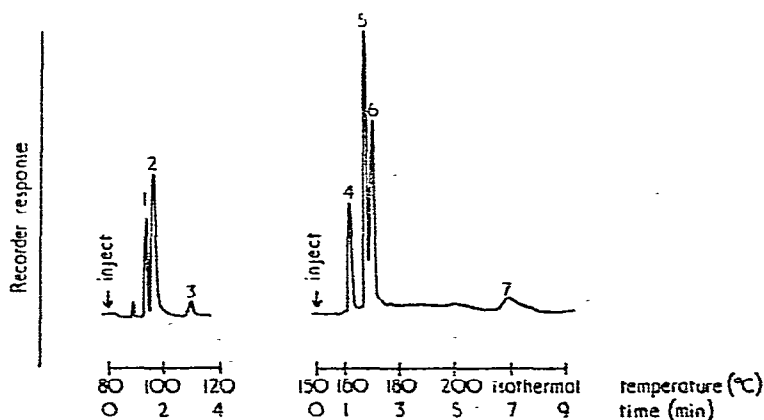

Fig. 1. Separation of carbamates in mixtures (20 ng of each compound) by on-column derivatisation with TMAH and temperature programming to 200°. Column, 0.5% Carbowax 20M + 5% SE-30; inlet pressure of nitrogen carrier gas, 10 p.s.i. 1 = Aldicarb; 2 = methomyl; 3 = DS-15647; 4 = Tirpate; 5 = oxamyl and DS-15647 sulphone, unresolved; 6 = methiocarb; 7 = methiocarb sulphone. The peak eluting at 89° is aldicarb nitrile.

which is then methylated. Carbamates having at least one unsubstituted position on the nitrogen are rapidly hydrolysed in aqueous alkali, and Ebing[22] observed that GLC injection of substituted-phenyl N-methylcarbamates with aqueous ammonia produced the corresponding phenols. Authentic oximes or phenols injected with TMAH gave derivatives of the same retention time as those produced similarly from the carbamates. Although the procedure gave similar yields of derivatives from both the carbamates and their hydrolysis products, this is perhaps fortuitous, especially for the aldoximecarbamates which can be degraded by competing reactions not readily available to their oximes.

The procedure gave reproducible results, six consecutive injections of oxamyl (23 ng) with TMAH giving a standard deviation of 4.9% about the mean peak height. GLC peak heights for oxamyl injected with TMAH and oxamyl methoxime fell on the same calibration curve (Fig. 2) over the range 10-250 picomoles.
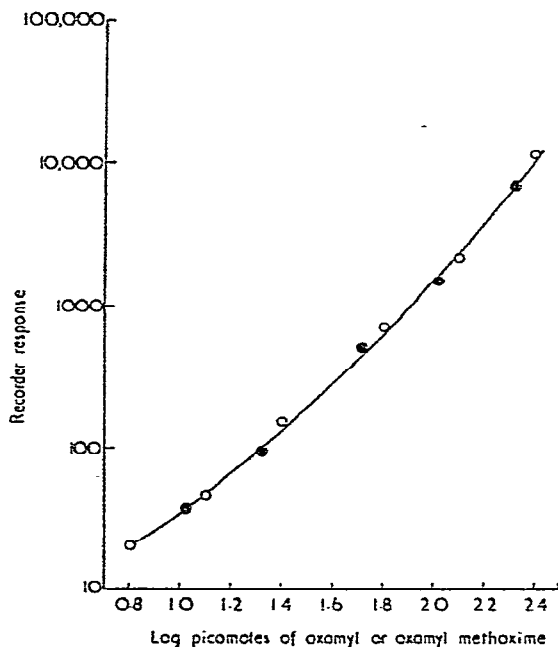

Fig. 2. Log-log calibration curve using the flame photometric detector in the sulphur mode. Column, 0.5% Carbowax 20M + 5% SE-30, maintained at 150°. O = Oxamyl methoxime; ● = oxamyl plus TMAH.

Few problems were encountered with the procedure although apparent yields of oxamyl methoxime could be reduced to about 80% if the injection port became contaminated with rubber fragments from the septum or carbonised involatiles from crop extracts, etc., and, at oven temperatures of less than 110°, injections made within 10 min of a previous TMAH-containing injection gave slightly reduced peak heights. Injections of the preformed derivatives with TMAH also gave similarly reduced responses under these conditions, probably caused by volatiles generated by the thermal decomposition of the TMAH[23] bleeding slowly into the detector and quenching the

sulphur emission[24]. Some accumulation of TMAH does occur in the GLC injection port, as injection of oxamyl alone following a series of injections with TMAH produced an appreciable peak of the methoxime. Conditioning the chromatograph overnight at the normal operating conditions removed this "memory effect".

Oxamyl has been estimated routinely in a wide range of soil and crop samples using on-column derivatisation with TMAH. This method does not distinguish between carbamates and their hydrolysis products, and the latter must be removed by "clean-up" procedures if estimation of the carbamates alone is required. Although this study has been confined to the assay of sulphur-containing carbamates using the highly sensitive and selective flame photometric detector, the derivatisation procedure should be applicable to the GLC analysis of other carbamates using different detectors.

ACKNOWLEDGEMENTS

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