

- Chem.* **211**, 907-13 (1954).
 (9) Plaisted, P. H., *Contrib. Boyce Thompson Inst.* **20**, 83-107 (1959).
 (10) Vanderzant, E. S., *J. Econ. Entomol.* **56**, 357-62 (1963).

- (11) Vanderzant, E. S., Davich, T. B., *Ibid.*, **54**, 923-8 (1961).
 (12) Vanderzant, E. S., Richardson, C. D., Davich, T. B., *Ibid.*, **52**, 1138-43 (1959).

Received for review February 28, 1963. Accepted May 13, 1964. Mention of proprietary products in this paper does not constitute their endorsement by the U. S. Department of Agriculture.

INSECTICIDE ACTIVITY AND STRUCTURE

N-Alkyl Carbamates as Insecticides and Pyrethrins Synergists

H. I. THAYER, R. J. HARTLE, and A. MALLIS
 New Products Division, Gulf Research & Development Co., Pittsburgh 30, Pa.

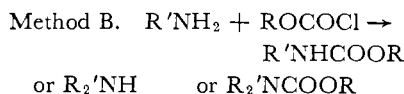
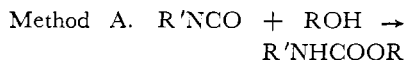
Of a series of *N*-alkyl carbamates three were found to show appreciable insecticidal activity against houseflies: 4-indanyl, 5-indanyl, and 3,4-methylenedioxyphenyl *N*-methyl carbamate. Other carbamates which were not toxic were effective synergists for pyrethrins and allethrin against cockroaches and houseflies; one outstanding example of this type was 3,4-methylenedioxyphenyl *N*-butoxyethoxyethyl carbamate.

FOR some time certain carbamates have been known to possess physiological activity, but particular interest in this class of compounds as pesticides has grown rapidly since 1947 (19, 20). Various aryl and heterocyclic esters of *N*-alkyl and *N,N*-dialkyl carbamates have been shown to be toxic to houseflies as well as aphids, thrips, mosquito larvae, and other insects (7, 11, 12, 18, 27, and others). Also, the pyrethrins synergistic activity of carbamates to houseflies has been investigated and reported in a few instances. Prill (24, 25) has claimed certain 3,4-methylenedioxyphenylalkyl *N*-alkyl carbamates to be pyrethrins synergists. In contrast, several 3,4-methylenedioxyphenyl *N*-aryl carbamates show only slight synergism for pyrethrins (7, 2, 9).

Our original interest was in determining the effectiveness of the indanyl moiety in a carbamate type of insecticide or pyrethrins synergist. Because the 5-indanyl and 3,4-methylenedioxyphenyl groups are similar to one another with respect to the spatial relations of their atoms, indanyl derivatives might show insecticidal or synergistic activity comparable to that of 3,4-methylenedioxyphenyl derivatives. Our second objective was to determine the effectiveness of Oxo-octyl—that is, mixture of octyl isomers obtained in the Oxo process (17)—derivatives of carbamates. Both the alcohol and the amine mixtures were used in the preparation of these compounds.

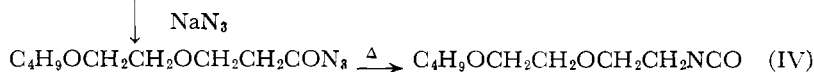
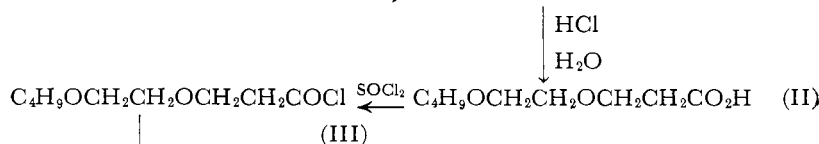
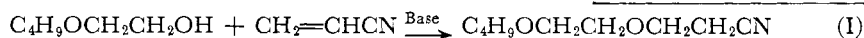
Experimental

Syntheses. The compounds evaluated in this study, listed in Tables I and II, were synthesized by one of two methods:



Choice of Method A or B was determined by the availability of starting materials. Methyl, ethyl, *n*-butyl, *n*-undecyl, and *n*-octadecyl isocyanates were obtained from commercial sources. *n*-Heptyl and *n*-butoxyethoxyethyl isocyanates were prepared from acid chlorides (16). With the exception of 3,4-methylenedioxybenzyl alcohol (5), all of the alcohols, amines, and phenols were purchased.

Method A. The synthesis of butoxyethoxyethyl isocyanate (IV) and the carbamate, S-16, formed by the reaction of IV with 3,4-methylenedioxyphenol (sesamol) illustrates this procedure. The reactions involved in the preparation of the isocyanate are as follows (6):



3-(2-*n*-BUTOXYETHOXY)PROPIONITRILE (I). This compound was prepared by the base-catalyzed addition of butoxyethanol to acrylonitrile following the general procedure of Bruson (3).

To a mixture of 237 grams (2 moles) of butoxyethanol (dried over calcium hydride and distilled) and 3 ml. of a

35% solution of Triton B in methanol were added 106 grams (2 moles) of freshly distilled acrylonitrile. The addition was carried out at a rate to maintain a reaction temperature of 45° to 50° C. The mixture was stirred at room temperature for 1 hour after addition was complete and then made slightly acidic with acetic acid and filtered. The filtrate was distilled at reduced pressure to yield 293 grams (85%) of 3-(2-*n*-butoxyethoxy)-propionitrile, boiling at 95-97° C. at 1 to 2 mm.; $n_D^{25} = 1.4280$.

Analysis. Calculated for $C_9H_{17}O_2N$: C, 63.12; H, 10.00; N, 8.18. Found: C, 63.07; H, 10.17; N, 7.99.

3-(2-*n*-BUTOXYETHOXY)PROPIONIC ACID (II). 3-(2-*n*-Butoxyethoxy)propionitrile (257 grams, 1.5 moles) was added dropwise with stirring to 300 grams of concentrated hydrochloric acid which was held at 70° C. The mixture was stirred at this temperature for 3 hours, followed by 30 minutes of heating at 100° C. Water was then removed from the reaction mixture in a flash

evaporator. The by-product, ammonium chloride, was separated by filtration and washed with ether. The solvent was distilled from the filtrate, and the product was distilled at reduced pressure to yield 237 grams (83%) of 3-(2-*n*-butoxyethoxy)propionic acid (boiling point, 134° C. at 1.5 mm.).

Analysis. Calculated for $C_9H_{18}O_4$: neutralization equivalent, 190.2; C, 56.82; H, 9.54. Found: neutralization equivalent, 210.0; C, 56.55; H, 9.26.

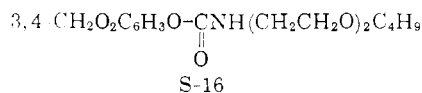
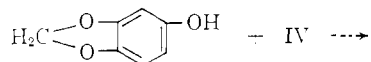
3-(2-*n*-BUTOXYETHOXY)PROPIONYL CHLORIDE (III). 3-(2-*n*-Butoxyethoxy)propionic acid (214 grams, 1.13 moles) was added dropwise with stirring to 180 grams of thionyl chloride held at 30° to 35° C. After addition was complete, 30 grams of thionyl chloride were added and the mixture was stirred at 35° C. for 45 minutes. Distillation of the reaction product through a 10-inch Vigreux column gave 194 grams (82%) of 3-(2-*n*-butoxyethoxy)propionyl chloride, boiling at 91–92° C. at 2 mm.

Analysis. Calculated for $C_9H_{17}O_3Cl$: C, 51.79; H, 8.21. Found: C, 51.88; H, 8.19.

2-(2-*n*-BUTOXYETHOXY)ETHYL ISOCYANATE (IV). A solution of 46 grams (0.7 mole) of sodium azide in 125 ml. of water was chilled to 5° C. in an ice bath. 3-(2-*n*-Butoxyethoxy)propionyl chloride (105 grams, 0.5 mole) in 250 ml. of anhydrous ethyl ether was added to the azide solution with rapid stirring at such a rate that the temperature did not exceed 10° C. The reaction mixture was stirred at 5° to 10° C. for an additional 2 hours. The aqueous layer was then removed through a suction tube and extracted once with ether. The ether extract was combined with the original ether layer and the total dried over sodium sulfate in an ice bath for 15 minutes. The ether solution was then added in a slow stream with stirring to 500 ml. of dry benzene (c. p. grade) held at 60° to 70° C. in a water bath. The addition rate was regulated to maintain a steady evolution of nitrogen over a 2-hour period. After removal of solvents, the residual liquid was distilled at reduced pressure to give 74 grams (79%) of 2-(2-*n*-butoxyethoxy)ethyl isocyanate (boiling point, 84–86° C. at 2 mm.).

Analysis. Calculated for $C_9H_{17}O_3N$: C, 57.73; H, 9.15; N, 7.48. Found: C, 57.40; H, 8.94; N, 7.47.

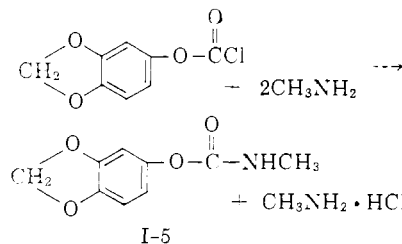
3,4-METHYLENEDIOXYPHENYL *N*-BUTOXYETHOXYETHYL CARBAMATE, S-16



(74). A solution of 62 grams (0.45 mole) of sesamol in 400 ml. of dry benzene was refluxed. After traces of water were removed by separation in a Dean-Stark trap, 73 grams (0.39 mole) of 2-(2-*n*-butoxyethoxy)ethyl isocyanate and 0.1 ml. of triethylamine were added. The mixture was refluxed for 6 hours, then cooled at room temperature and washed successively with 200 ml. each of 1.5% sodium hydroxide solution, water, dilute hydrochloric acid, and water. After the benzene solution had been dried over sodium sulfate, solvent was removed in a flash evaporator, leaving 122 grams (96%) of 3,4-methylenedioxyphenyl *N*-butoxyethoxyethyl carbamate, a pale yellow liquid; $n_D^{25} = 1.5063$.

Analysis. Calculated for $C_{16}H_{23}O_3N$: C, 59.06; H, 7.13; N, 4.31. Found: C, 58.65; H, 7.08; N, 4.08.

Method B. Of the two methods of synthesis, only Method B is feasible for *N,N*-disubstituted carbamates. A satisfactory method for preparing chloroformates, required in Method B, has been described by Strain *et al.* (29). An example of this method is the preparation of 3,4-methylenedioxyphenyl *N*-methyl carbamate, I-5 (73), by the reaction of appropriate chloroformate and amine.



A mixture of 80 grams (1 mole) of 40% aqueous methylamine solution and 200 ml. of ethyl ether (alcohol-free) was chilled to 0° C. in an ice-salt bath. A solution of 55 grams (0.28 mole) of 3,4-methylenedioxyphenylchloroformate (b.p., 112–14° C./4.5 mm.) in 150 ml. of ethyl ether was added dropwise to the cold amine solution with rapid stirring. Temperature was maintained at 0° to 5° C. during the addition, which required 1 hour. The ether layer was then extracted with water and dilute hydrochloric acid. Evaporation of ether followed by drying in vacuo gave 43 grams (78%) of 3,4-methylenedioxyphenyl *N*-methyl carbamate as colorless prisms. Recrystallized from benzene (m.p., 108–109° C.).

Analysis. Calculated for $C_9H_9O_3N$: N, 7.18. Found: N, 7.21.

Insecticidal Tests

Houseflies [*Musca domestica* (L.)]. The screening method (mist tower test) used was first described by Campbell, Barnhart, and Hutzel (4). All compounds were tested in a solution of odorless Gulsol No. 10 (GSN), a typical odorless-type household insecticide base oil (specific gravity 0.78, $n_D^{20} 1.43$, distillation range 380° to 480° F., approximately 90% paraffinic). In cases of limited solubility, absolute ethanol or Oxodecyl alcohol was used as cosolvent, usually in an amount less than 5% by volume. These auxiliary solvents were shown not to contribute to synergism or insecticidal activity at a 5% level by themselves or in combination with chemicals under test. Compounds were tested in combination with pyrethrins to determine synergistic activity, as well as evaluated alone to detect insecticidal activity (Tables I and II). The more promising materials also were tested by the Peet-Grady method (27).

Cockroaches [*Blattella germanica* (L.), *Periplaneta americana* (L.), and *Blattella orientalis* (L.)]. Toxicity of several of the carbamates alone and in combina-

tion with pyrethrins against cockroaches was determined. The CSMA official cockroach spray test method (28) was used to evaluate the test solutions; the oil-base sprays were applied by a standard procedure to adult German male roaches. Twenty roaches were used per test unit; three or four replicates constituted a test and their averages are summarized in Table III.

In the second screening procedure, called the racetrack method (22), three test insects—adult males of German roaches, nymphs of oriental roaches, and nymphs of American roaches—were used. Experimental insecticide I-5 was evaluated by this method (Table III).

Discussion

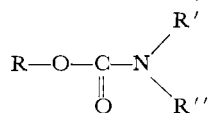
Insecticidal Activity. Of the group of compounds studied, seven which showed definite insecticidal activity when tested against houseflies were of the aryl *N*-alkyl carbamate class (see Table I). The three most active compounds, all *N*-monomethyl carbamates, in order of decreasing effectiveness, were: 3,4-methylenedioxyphenyl *N*-methyl carbamate (I-5), 5-indanyl *N*-methyl carbamate (I-2), and 4-indanyl *N*-methyl carbamate (I-1) (73). The *N*-ethyl derivatives were considerably less toxic, and *N*-isopropyl and *N*-butyl carbamates showed practically no toxicity to houseflies. The two *N,N*-dimethyl carbamates (I-3 and I-6) evaluated were approximately as toxic as their *N*-monomethyl isomers. A decrease in insecticidal activity has been reported for other aryl *N*-alkyl carbamates (78) when the *N*-substituent is lengthened or two substituents are present on the *N*-atom.

In our screening test 5-indanyl *N*-methyl carbamate (I-2) was more effective than the commercial insecticide Sevin (trade-mark Union Carbide Chemicals Co., 1-naphthyl *N*-methyl carbamate) against houseflies. The 4-indanyl *N*-methyl carbamate (I-1) was less toxic than Sevin. 3,4-Methylenedioxyphenyl *N*-methyl carbamate (I-5) was more toxic than the indanyl derivatives or Sevin; I-5 also was superior to dimetan (5,5-dimethyldihydroresorcinol *N,N*-dimethyl carbamate) and Pyrolan [trade-mark Geigy Chemical Corp., 1-phenyl-3-methylpyrazolyl-(5) *N,N*-dimethyl carbamate]. The *N*-methyl carbamate of 3,4-methylenedioxybenzyl alcohol (S-22) was not toxic to houseflies (Table II).

To evaluate the possibility of using I-5 in commercial household fly sprays, a Peet-Grady test (Table IV) was conducted. At the concentration level of 50 mg. per 100 ml. I-5 was less effective than pyrethrins but showed a higher kill than Sevin.

Comparative tests by the CSMA official cockroach spray test method showed Sevin to be superior to I-5

Table I. Properties of Substituted Aryl *N*-Alkyl Carbamates



Compound	R	R'	R''	Preparation Method	M.P., °C.	Nitrogen, %		Pesticidal Activity against Houseflies (4)	
						Calcd.	Found	Insecticide % kill (24 hr.) ^a	Synergist rating ^b
I-1	2,3-CH ₂ CH ₂ CH ₂ C ₆ H ₅	CH ₃	H	B	87-89	7.33	7.41	80	...
S-1	2,3-CH ₂ CH ₂ CH ₂ C ₆ H ₅	CH ₃	CH ₃	B	Liquid b.p., 115-118/1.1 mm.	6.83	6.52	4	F
S-2	2,3-CH ₂ CH ₂ CH ₂ C ₆ H ₅	<i>n</i> -C ₇ H ₁₅	H	A	Liquid	5.09	5.07	9	F
I-2	3,4-CH ₂ CH ₂ CH ₂ C ₆ H ₅	CH ₃	H	A and B	91	7.33	7.40	95; 85(500); 35(100)	...
I-3	3,4-CH ₂ CH ₂ CH ₂ C ₆ H ₅	CH ₃	CH ₃	B	61	6.83	6.66	45	...
I-4	3,4-CH ₂ CH ₂ CH ₂ C ₆ H ₅	C ₂ H ₅	H	B	85-87	6.83	6.85	43	...
S-3	3,4-CH ₂ CH ₂ CH ₂ C ₆ H ₅	(CH ₃) ₂ CH	H	B	98-99	6.39	6.37	3	F
S-4	3,4-CH ₂ CH ₂ CH ₂ C ₆ H ₅	<i>n</i> -C ₄ H ₉	H	A	56-58	5.98	5.71	1	F
S-5	3,4-CH ₂ CH ₂ CH ₂ C ₆ H ₅	<i>n</i> -C ₇ H ₁₅	H	A	49	5.09	5.02	9	F
S-6	C ₆ H ₅	<i>n</i> -C ₇ H ₁₅	H	A	Liquid	5.96	5.78	3	F
S-7	5-CH ₃ -2-(CH ₃) ₂ CHC ₆ H ₃	<i>n</i> -C ₇ H ₁₅	H	A	Liquid	4.81	4.48	...	F
S-8	2,4-Cl ₂ C ₆ H ₃	<i>n</i> -C ₇ H ₁₅	H	A	59	4.60	4.66	3	F
S-9	3,4-C(CH ₃) ₂ CH ₂ CH ₂ C(CH ₃) ₂ C ₆ H ₃	<i>n</i> -C ₇ H ₁₅	H	A	Liquid	4.06	3.95	...	S
I-5	3,4-OCH ₂ OC ₆ H ₅	CH ₃	H	B	108-109	7.18	7.21	100; 100(200); 80(100)	...
I-6	3,4-OCH ₂ OC ₆ H ₅	CH ₃	CH ₃	B	78	6.64	7.37	48	...
I-7	3,4-OCH ₂ OC ₆ H ₅	C ₂ H ₅	H	B	92-93	6.70	6.64	46	...
S-10	3,4-OCH ₂ OC ₆ H ₅	<i>n</i> -C ₄ H ₉	H	A	85-86	5.90	6.18	8	G
S-11	3,4-OCH ₂ OC ₆ H ₅	Oxo-C ₈ H ₁₇	H	B	Liquid	4.78	4.50	6	G
S-12	3,4-OCH ₂ OC ₆ H ₅	<i>n</i> -C ₁₁ H ₂₃	H	A	96-97	4.18	4.23	2	G
S-13	3,4-OCH ₂ OC ₆ H ₅	2-CH ₃ OC ₂ H ₄	H	B	Liquid	5.86	5.00	4	G
S-14	3,4-OCH ₂ OC ₆ H ₅	3-CH ₃ OC ₃ H ₆	H	B	63	5.53	5.45	3	G
S-15	3,4-OCH ₂ OC ₆ H ₅	3-(CH ₃) ₂ CHOC ₃ H ₆	H	B	73	4.98	5.45	15	G
S-16	3,4-OCH ₂ OC ₆ H ₅	C ₄ H ₉ (OCH ₂ CH ₂) ₂	H	A	Liquid	4.31	4.08	5	G
Dimetan	5,5-(CH ₃) ₂ CCH ₂ C(=O)CH=C	CH ₃	CH ₃	61; 52(500)	...
Pyrolan	1-C ₆ H ₅ -N=N=C(3-CH ₃)CH=C	CH ₃	CH ₃	75; 55(500)	...
Sevin	2,3-(CH=CH) ₂ C ₆ H ₃	CH ₃	H	90; 52(500)	...

^a Compounds usually were tested at a concentration of 1000 mg./100 ml.; numbers in parentheses indicate other concentrations in mg./100 ml. at which compound was evaluated.

^b Synergist ratings were determined by comparison of results obtained with test solution (1000 mg. test compound + 50 mg. pyrethrins/100 ml.) and those obtained with pyrethrins only (50 mg./100 ml.). The difference in "kill value," Δ, was taken to be an indication of synergistic activity of the compound. A scale of letter ratings is used: N, Δ = 0-5%; S, Δ = 6-15%; F, Δ = 16-35%; and G, Δ = 36 or greater %.

in killing German male cockroaches (Table III). When evaluated against this same species of cockroach by the Gulf racetrack method Sevin and I-5 were about equally effective. This also was true for tests run with nymphs of the American and oriental cockroach.

Pyrethrins Synergistic Activity. Much less has been published concerning

carbamates as synergists for pyrethrins or allethrin than has been reported on insecticidal carbamates. Previous investigators have found 3,4-methylenedioxyphenyl *N*-aryl carbamates to show little or no pyrethrins synergism against houseflies (7, 2, 9, 26); in contrast, 3,4-methylenedioxyphenylalkyl *N*-alkyl carbamates were reported to have pronounced synergistic activity when

tested in combinations containing pyrethrins or allethrin (24, 25). The 11 most effective synergists of the group of compounds we have screened contained either a 3,4-methylenedioxyphenyl or 3,4-methylenedioxybenzyl group and were *N*-alkyl carbamates or *N*-alkoxyalkyl carbamates (Table V). The corresponding indanyl derivatives showed definite synergistic properties but were

Table II. Properties of Alkyl *N*-Alkyl Carbamates

$$\begin{array}{c} \text{R}' \\ | \\ \text{R}-\text{O}-\text{C}-\text{N} \\ || \quad | \\ \text{O} \quad \text{R}'' \end{array}$$

Compound	R	R'	R''	Preparation Method	M.P., °C.	Nitrogen, %		Pesticidal Activity against Houseflies (4)	
						Calcd.	Found	Insecticide % kill (24 hr.) ^a	Synergist rating ^b
S-17	CH ₃	<i>n</i> -C ₄ H ₉	H	A	Liquid, b.p., 98/25 mm.	10.67	10.87	3	S
S-18	C ₂ H ₅	(CH ₃) ₂ CH	H	B	Liquid, b.p., 88/25 mm.	10.67	10.24	1	S
S-19 ^c	C ₂ H ₅	CH ₂ (CH ₂) ₄ CH	H	...	58	8.18	8.22	3	F
S-20 ^a	C ₂ H ₅	<i>tert</i> -C ₃ H ₁₇	H	...	Liquid	6.96	7.71	2	S
S-21	<i>n</i> -C ₈ H ₁₇	CH ₃	H	B	Liquid, b.p., 120/25 mm.	9.63	9.38	...	S
S-22	<i>n</i> -C ₈ H ₁₇	CH ₃	CH ₃	B	Liquid, b.p., 85/10 mm.	8.77	8.68	3	F
S-23	C ₆ H ₅ (C ₂ H ₅)CHCH ₂	CH ₃	H	B	Liquid, b.p., 114/5 mm.	7.47	7.50	...	S
S-24	Oxo-C ₈ H ₁₇	C ₂ H ₅	H	A	Liquid	6.96	7.80	3	F
S-25	Oxo-C ₈ H ₁₇	<i>n</i> -C ₄ H ₉	H	A	Liquid, b.p., 104-108/10 mm.	6.12	5.87	2	F
S-26	Oxo-C ₈ H ₁₇	<i>n</i> -C ₇ H ₁₅	H	A	Liquid	5.18	5.23	3	F
N-1	Oxo-C ₈ H ₁₇	<i>n</i> -C ₁₈ H ₃₇	H	A	81	3.27	3.77	...	N
N-2	<i>n</i> -C ₁₂ H ₂₅	CH ₃	H	B	54	5.75	6.00	...	N
N-3	<i>n</i> -C ₁₂ H ₂₅	3-(C ₂ H ₅) ₂ NC ₃ H ₆	H	B	Liquid	8.18	7.20	...	N
S-27	3,4-OCH ₂ OC ₆ H ₃ CH ₂	CH ₃	H	B	68	6.99	6.60	3	G
S-28	3,4-OCH ₂ OC ₆ H ₃ CH ₂	C ₂ H ₅	H	B	48	3	G
S-29	3,4-OCH ₂ OC ₆ H ₃ CH ₂	<i>n</i> -C ₄ H ₉	H	B	Liquid	4.60	5.57	5	G
S-30	3,4-OCH ₂ OC ₆ H ₃ CH ₂	C ₄ H ₉ (OCH ₂ CH ₂) ₂	H	A	Liquid	4.13	4.21	27	G

^a Compounds evaluated at concentrations of 1000 mg./100 ml.

^b Rating scale as in Table I.

^c Purchased from Aldrich Chemical Co., Inc.

not as effective—for example, S-4 *vs.* S-10 (Table I); thus, the possibility of substituting the indanyl moiety for the methylenedioxyphenyl group does not appear to be commercially promising.

Of the derivatives tested, 3,4-methylenedioxyphenyl *N*-butoxyethoxyethyl carbamate (S-16) was the most effective pyrethrins synergist. Another *N*-alkoxyalkyl derivative, S-15, was effective and even the *N*-Oxo-octylcarbamate, S-11, showed fair activity (75). The effectiveness of S-16 was investigated further by tests in the Peet-Grady chamber (Table IV). At a synergist-pyrethrins ratio of 3 to 4 (37.5 mg. S-16), S-16 was about as effective as piperonyl butoxide (3,4-methylenedioxy-6-propylbenzyl butyldiethylene glycol ether); with allethrin, S-16 also was comparable to piperonyl butoxide. Other carbamate synergists evaluated by the Peet-Grady test were S-11 and S-12; although effective as pyrethrins synergists, S-16 surpassed them.

Another pair of tests run in the Peet-Grady chamber, a combination of the carbamate I-5 and pyrethrins and one of Sevin and pyrethrins, showed I-5 to be synergizing the pyrethrins slightly. The kill for the combination containing Sevin was not even additive. The

Table III. Evaluation of *N*-Alkyl Carbamates against Cockroaches

Compound	Concn., Mg./100 ml. ^a	Pyrethrins, Mg./100 ml. ^a	% Knockdown		% Kill, 48 Hr. ^b
			10 min.	30 min.	
A. CSMA Official Cockroach ^a Spray Test Method (28)					
I-5	1000	...	0	60	67
Sevin	1000	...	97	98	98
...	...	50	96	96	12
S-16	250	...	0	0	5
S-16	250	50	100	100	86
Piperonyl butoxide	250	...	0	0	7
Piperonyl butoxide	250	50	100	100	41
...	...	50	100	100	34
S-16	1000	100 ^c	95	93	84
...	...	100 ^c	54	38	9
B. Gulf Racetrack Method (22); All Test Compounds Evaluated at 1000 Mg./100 ml.					
Test Insect					
I-5	American nymphs	...	0	40	100
Sevin	American nymphs	...	3	100	100
...	American nymphs	50	5	2	30 ^d
I-5	Oriental nymphs	...	0	28	97
Sevin	Oriental nymphs	...	28	97	98
...	Oriental nymphs	50	2	18	20 ^d
I-5	German males	...	2	90	98
Sevin	German males	...	68	100	100
...	German males	50	97	92	68 ^d

^a German male adult cockroaches were test insect. Spray solvent GSN.

^b Duration of tests by either method was 144 hr.; in no instance was there any significant change in % kill at 48 *vs.* 144 hr.

^c Allethrin substituted for pyrethrins.

^d Check tests also were run on spray solvent. % kills were: American nymph, 3%; oriental nymph, 0%; German males, 30%.

Table IV. N-Alkyl Carbamates Tested against Houseflies in Peet-Grady Chamber (27)

	Compound	Concn., Mg./100 ml.	Allethrin (A) or Pyrethrins (P), Mg./100 ml.	% Kill (Av.), ^a 24 Hr.
I-5	3,4-Methylenedioxyphenyl N-methyl carbamate	50 ^b	...	28
I-5	3,4-Methylenedioxyphenyl N-methyl carbamate	47.5 ^b	50 P	74
	Sevin	50 ^b	...	19
	Sevin	47.5 ^b	50 P	48
	50 P	41
S-11	3,4-Methylenedioxyphenyl N-oxo-octyl carbamate	100 ^c	50 P	63
S-12	3,4-Methylenedioxyphenyl N-undecyl carbamate	100 ^c	50 P	49
S-16	3,4-Methylenedioxyphenyl N-butoxyethoxyethyl carbamate	100 ^c	50 P	92
S-16	3,4-Methylenedioxyphenyl N-butoxyethoxyethyl carbamate	37.5 ^d	50 P	79
S-16	3,4-Methylenedioxyphenyl N-butoxyethoxyethyl carbamate	37.5 ^d	50 A	72
	Piperonyl butoxide	37.5	50 P	82
	Piperonyl butoxide	37.5	50 A	73
	OTI ^e	...	108 P	49

^a % knockdowns after 10 min. were 95+ % except for I-5 and Sevin evaluated alone at 50 mg./100 ml.; knockdown was 31 % in each of these instances.

^b Solvent 50:50 (vol.) GSN-absolute ethanol.

^c Solvent 95:5 mixture of GSN-absolute ethanol.

^d Solvent 95:5 mixture of GSN-decyl alcohol.

^e OTI = official test insecticide.

Table V. Screening of N-Alkyl Carbamates as Pyrethrins Synergists against Houseflies (4)

		Test solutions contained compound + 50 mg. pyrethrins/100 ml. GSN			
Compound	Name	Synergist Rating			
		Mg./100 ml.	Plus kill ^a	Mg./100 ml.	Plus kill ^a
S-10	3,4-Methylenedioxyphenyl N-butyl carbamate	300	46
S-11	3,4-Methylenedioxyphenyl N-oxo-octyl carbamate	250	61	100	32
S-12	3,4-Methylenedioxyphenyl N-undecyl carbamate	250	45	100	33
S-13	3,4-Methylenedioxyphenyl N-methoxyethyl carbamate	100	28
S-14	3,4-Methylenedioxyphenyl N-methoxypropyl carbamate	100	32
S-15	3,4-Methylenedioxyphenyl N-isopropoxypropyl carbamate	100	58
S-16	3,4-Methylenedioxyphenyl N-butoxyethoxyethyl carbamate	250	73	100	65
S-27	3,4-Methylenedioxybenzyl N-methyl carbamate	300	28
S-28	3,4-Methylenedioxybenzyl N-ethyl carbamate	300	30
S-29	3,4-Methylenedioxybenzyl N-butyl carbamate	300	34
S-30	3,4-Methylenedioxybenzyl N-butoxyethoxyethyl carbamate	100	59

^a Plus kill = % kill observed for test solution - % kill for 50 mg. pyrethrins, which ranged from 31-51 % kill.

possibility that 3,4-methylenedioxyphenyl N-methyl carbamate might have both synergistic and insecticidal activity has been suggested by Metcalf, Fukuto, and Winton (27); results of our test would seem to support this viewpoint.

Synergist S-16 also was evaluated against German cockroaches. In this application it was considerably better than piperonyl butoxide as a pyrethrins synergist (5 to 1 ratio, 250 mg. of synergist). When used with allethrin, a ratio of 10 to 1 (1000 mg. of synergist)

was necessary to obtain the same kill range as with pyrethrins at a 5 to 1 ratio.

Additional Synergistic Studies. Since the N-alkyl carbamates chosen for study showed both insecticidal and synergistic activity, a few tests were made to investigate combinations of commercial synergists with a carbamate insecticide and also mixtures of carbamate-synergists and carbamate-insecticides. Although our work in these areas is not completed, these findings are being reported at this time.

Synergism of certain carbamate-insecticides was reported some time ago by other investigators—for example (19, 21, 23). Our tests with I-5 against houseflies by the mist tower procedure showed that piperonyl butoxide, piperonyl cyclonene {mixture of 3-n-hexyl-5-(3,4-methylenedioxyphenyl)-2-cyclohexenone and 6-carbomethoxy-3-n-hexyl-5-(3,4-methylenedioxyphenyl)-2-cyclohexenone}, sulfoxide (n-octyl sulfoxide of isosafrole), MGK 264 [N-(2-ethylhexyl)-bicyclo-[2.2.1]-5-heptene-2,3-dicarboximide], and Sexoxane [trade-mark of Shulton, Inc., 2-(2-ethoxyethoxy)-ethyl-3,4-methylenedioxyphenyl acetal of acetaldehyde] enhanced the activity of the insecticide when mixtures were evaluated in which the ratio of synergist to insecticide was 10 to 1 (600 mg. of synergist). The relative decreasing order of synergist effectiveness was in the order named and ranged from 24 to 4% enhancement in the “% kill” value. Fukuto *et al.* (8) have reported I-5 not to be synergized by piperonyl butoxide when evaluated by a topical application method. Differences in the synergist-insecticide ratio and the methods of application may account for this variance.

Two combinations of carbamate insecticide and carbamate synergists were investigated as housefly toxicants. In one instance (I-2 + S-6) no synergism was observed, but in the case of I-5 and a more potent pyrethrins synergist, S-10, the toxicity of the mixture showed an increase of 16% in the “% kill” for a 10 to 1 mixture of synergist-insecticide (600 mg. of synergist). This type of synergistic combination should not be confused with that reported by Gordon and Eldefrawi (10), which they termed “analog synergism” and which involves two carbamate-insecticides rather than one carbamate-insecticide and one carbamate-synergist.

Summary

Forty N-alkyl carbamates were evaluated as insecticides and pyrethrins synergists. Seven were shown to have insecticidal properties, while 30 which had negligible insecticidal activity were pyrethrins synergists and three were inactive as insecticides or synergists toward the housefly. More particularly, indanyl N-alkyl carbamates were found to be less effective insecticides or synergists than their 3,4-methylenedioxybenzyl N-alkyl carbamates showed greater synergism for pyrethrins than carbamate esters of alkanols.

Acknowledgment

The authors thank A. C. Miller and J. P. Pellegrini, Jr., for their helpful discussions and interest in this problem.

Literature Cited

- (1) Beroza, M., *J. Agr. Food Chem.* **4**, 49 (1956).
- (2) Beroza, M., Berthel, W. F., *Ibid.*, **5**, 855 (1957).
- (3) Bruson, H. A., "Organic Reactions," Vol. V, p. 110, Wiley, New York, 1949.
- (4) Campbell, F. L., Barnhart, C. S., Hutzel, J. M., *Soap Sanit. Chemicals* **17**, 105, 109, 113, 115 (1941).
- (5) Davidson, D., Bogert, M. T., *J. Am. Chem. Soc.* **57**, 905 (1935).
- (6) Ek, A., Hartle, R. J., Gulf Research & Development Co., unpublished information.
- (7) Ferguson, G. P., Alexander, C. C., *J. Agr. Food Chem.* **1**, 888 (1953).
- (8) Fukuto, T. R., Metcalf, R. L., Winton, M. Y., Roberts, P. A., *J. Econ. Entomol.* **55**, 341 (1962).
- (9) Gersdorff, W. A., Piquett, P. G., Beroza, M., *J. Agr. Food Chem.* **4**, 858 (1956).
- (10) Gordon, H. T., Eldefrawi, M. E., *J. Econ. Entomol.* **53**, 1004 (1960).
- (11) Gysin, H., *Chimia (Switz.)* **8**, 205 (1954).
- (12) Hansens, E. J., Bartley, C. E., *J. Econ. Entomol.* **46**, 372 (1953).
- (13) Hartle, R. J., Thayer, H. I. (to Gulf Research & Development Co.), U. S. Patent **2,951,850** (Sept. 6, 1960).
- (14) *Ibid.*, **2,990,320** (June 27, 1961).
- (15) *Ibid.*, **3,035,969** (May 22, 1962).
- (16) Horning, E. C., ed., "Organic Syntheses," Col. Vol. **III**, p. 846, Wiley, New York, 1955.
- (17) Hurd, V. N., Gwynn, B. H., *World Petrol. Congr., Proc. 5th., N. Y., 1959* **4**, 163 (pub. 1960).
- (18) Kolbezen, M. J., Metcalf, R. L., Fukuto, T. R., *J. Agr. Food Chem.* **2**, 864 (1954).
- (19) Metcalf, R. L., *Agr. Chem.* **16**, No. 6, 20 (1961).
- (20) Metcalf, R. L., "Organic Insecticides," pp. 317-30, Interscience, New York, 1955.
- (21) Metcalf, R. L., Fukuto, T. R., Winton, M. Y., *J. Econ. Entomol.* **53**, 828 (1960).
- (22) Miller, A. C., Mallis, A., Easterlin, W. C., *Ibid.*, **47**, 23 (1954).
- (23) Moorefield, H. H., *Contribs. Boyce Thompson Inst.* **19**, 501 (1958).
- (24) Prill, E. A. (to Boyce Thompson Institute for Plant Research), U. S. Patent **2,773,062** (Dec. 4, 1956).
- (25) *Ibid.*, **2,856,411** (Oct. 14, 1958).
- (26) Prill, E. A., Synerholm, M. E., *Contribs. Boyce Thompson Inst.* **14**, 221 (1946).
- (27) Soap and Chem. Specialties Blue Book, New York, pp. 225-7, 1962.
- (28) *Ibid.*, pp. 239, 240.
- (29) Strain, F., Bissinger, W. E., Dial, W. R., Rudoff, H., DeWitt, B. J., Stevens, H. C., Lanston, J. H., *J. Am. Chem. Soc.* **72**, 1254 (1950).

Received for review April 9, 1963. Accepted July 13, 1964. Presented in part at Meeting-in-Miniature, Central Pennsylvania Section, ACS, The Pennsylvania State University, University Park, Pa., March 15, 1958.

CARBAMATE INSECTICIDES

Gas Chromatographic Residue Determination of Sevin as Brominated 1-Naphthyl Acetate

WALTER H. GUTENMANN and DONALD J. LISK

Department of Entomology, New York State College of Agriculture, Cornell University, Ithaca, N. Y.

The insecticide, Sevin, has been determined in apples, broccoli, beans, corn, chicken, trout, bees, and soil at the 0.1-p.p.m. level by electron affinity gas chromatography. Following acetone extraction of samples and precipitation of interferences with ammonium chloride-phosphoric acid solution, Sevin is converted to a brominated 1-naphthyl acetate. This derivative is then chromatographed and determined by electron affinity detection. The recovery of Sevin from samples is good.

SEVIN (*N*-methyl-1-naphthyl carbamate) is one of the most widely used broad-spectrum carbamate insecticides. Methods for determining Sevin residues in crops, soil, poultry, fish, and other biological material are therefore essential.

Ralls and Cortes (3) brominated Sevin in a sealed tube with bromine in carbon tetrachloride to produce an electron-capturing derivative. The procedure was recommended as a screening method for detecting Sevin in green beans at the 1-p.p.m. level following a Florisil column cleanup, but not for quantitative analysis because of the production, in some instances, of mixed brominated derivatives. In the work reported, a procedure is described in which Sevin is hydrolyzed, brominated, and esterified in a single step to yield presumably brominated 1-naphthyl acetate. Following extraction of samples with acetone and precipitation of interferences with ammonium chloride in phosphoric acid solution (2), the brominated derivative is produced and chromatographed using

electron affinity determination. The method is sensitive to about 0.05 p.p.m. and has been successfully applied to analysis of apples, broccoli, beans, corn, chicken, trout, bees, and soil.

Procedure

Blend 25 grams of a representative subsample with distilled acetone and filter to a total volume of 100 ml. according to the procedure described earlier (7). The remainder of the isolation procedure is an adaptation of that of Niessen and Frehse (2). Transfer the total aqueous acetone extract to a 250-ml. separatory funnel and partition the solution for 1 minute successively with 100, 50, and 50 ml. of distilled chloroform. With samples low in moisture content, such as bees or soil, add about 20 ml. of water to the acetone extract before partitioning. Drain the chloroform layers through a 60° funnel containing filter paper and about 20 grams of anhydrous sodium sulfate and combine the layers in a 400-ml. beaker. Evaporate the solution to dryness using air and a 60° C. water bath.

Dissolve the residue in 15 ml. of acetone. Add 50 ml. of the aqueous precipitating solution containing 1.25 grams of ammonium chloride and 2.5 ml. of orthophosphoric acid per liter and allow the solution to stand for 30 minutes. Filter the solution through a Büchner funnel containing a 3-mm. layer of Celite 521 filter aid. Rinse the filter with 50 ml. of the precipitating solution. To the filtrate, add 20 ml. of a buffer solution (pH 12) containing 6.4 grams of citric acid, 3.5 grams of boric acid, 13.7 grams of sodium hydroxide, and 2.1 ml. of orthophosphoric acid per liter. Transfer the solution to a 250-ml. separatory funnel and partition successively with 75, 25, and 25 ml. of distilled carbon tetrachloride. Filter the carbon tetrachloride layers through sodium sulfate and evaporate the combined solutions to about 3 ml. Transfer the solution to a 10-ml. volumetric flask using carbon tetrachloride and evaporate the contents to dryness with air.

Hydrolysis, Bromination, and Esterification. Add 1 ml. of glacial acetic acid and 10 drops of concentrated sulfuric acid to the flask. Mix the