higher may be obtained by referring to Figure 6 and Table II. This gives only an estimate, however, and should not be relied upon alone. It is recommended, therefore, that the maintenance of thiono sulfur content, observed for small samples, should serve as the criterion for determining whether heat treatment of phosphorothioates at a given temperature and for a given time is apt to lead to decomposition.

The use of a continuous distillation process for removal of solvent from phosphorothioate insecticides allows short contact time at the distillation temperature and reduces the possibility of product decomposition to a minimum.

The decomposition described here may have been a factor bearing on the varying results which have been obtained in the past in comparing either the insect or mammalian toxicity of parathion or its homologs with their *S*-alkyl isomers, particularly in cases where the isomers were prepared by heat treatment of the parent insecticides. The absence of contact insecticidal activity, for instance, reported by Martin (*7*) for the methyl homolog of parathion after heating for 6 hours at 150° C. to nearly zero thiono sulfur content may have been due to the presence of mixed polymetaphosphates. It is estimated from the present studies that decomposition of the methyl homolog could occur in approximately 40 minutes at 150° C. Although the polymetaphosphates should be effective phosphorylating agents and thus should show in vitro inhibition of cholinesterase, their lack of solubility in benzene or ether should indicate low permeability to the insect cuticle and thus low contact insecticidal activity.

Acknowledgment

The authors are indebted to D. J. Salley and J. J. Carnes for their helpful suggestions, to G. A. Clarke, William Hart, and M. V. Norris for development of the modified thiono sulfur determination, to E. F. Williams for determination of the purity of materials by the cryoscopic method, and to members of the analytical staff for molecular weight, infrared, and other determinations.

Literature Cited

(1) Bright, N. F. H., Cuthill, J. C., and Woodbury, N. H., *J. Sci. Food Agr.* **1,** 344 (1950).
(2) Coates, H., and Topley, B., PB **95, 312 (BIOS 1808),** "Synthetic Insecticides," interrogation of Gerhard Schrader, 1947, Technical Information and Document Unit, 40 Cadogan Square, London, S. W. 1.
(3) Diggle, W. M., and Gage, J. C., *Biochem. J.* **49,** 491 (1951).
(4) Emmett, W. G., and Jones, H. O., *J. Chem. Soc.* **99,** 713 (1911).
(5) Goldschmidt, H., and Larsen, H., *Z. phys. Chem.* **71,** 437 (1910).
(6) Jura, W. H., *Anal. Chem.* **27,** 525 (1955).
(7) Martin, H., *J. Sci. Food Agr.* **1,** 163 (1950).
(8) Metcalf, R. L., and March, R. B., *J. Econ. Entomol.* **46,** 288 (1953).
(9) Morrill, H. L. (to Monsanto Chemical Co.), U. S. Patent **2,601,219** (June 17, 1952).
(10) Norris, M. V., Stamford Laboratories, American Cyanamid Co., private communication.
(11) O'Keeffe, K., and Averell, P. R., *Anal. Chem.* **23,** 1167 (1951).
(12) Sutherland, G. L., Stamford Laboratories, American Cyanamid Co., private communication.
(13) Topley, B., *Chemistry and Industry* **1950,** S859.
(14) Witschonke, C. R., *Anal. Chem.* **24,** 350 (1952).
(15) Woodcock, D., and Stringer, A., *Ann. Appl. Biol.* **38,** 111 (1951).

Received for review April 16, 1955. Accepted July 18, 1955. Division of Agricultural and Food Chemistry, Pesticides Subdivision, 127th Meeting, ACS, Cincinnati, Ohio, March 1955.

INSECTICIDE SYNERGISTS

3,4-Methylenedioxyphenoxy Compounds as Synergists for Natural and Synthetic Pyrethrins

MORTON BEROZA

Entomology Research Branch, Agricultural Research Service, U. S. Department of Agriculture, Beltsville, Md.

The discovery that a compound containing the 3,4-methylenedioxyphenoxy group produces a greater degree of synergism with pyrethrins than the corresponding compound containing a 3,4-methylenedioxyphenyl group, as in sesamolin and sesamin, led the author to synthesize new compounds containing the methylenedioxyphenoxy group as candidate synergists. This paper describes the preparation and properties of 66 of these compounds. In preliminary tests with the housefly by the turntable method, almost all the ethers, acetals, and sulfonates showed synergism, the urethans showed lesser activity, whereas the esters of carboxylic acids showed practically no synergism. Some of the compounds were sufficiently active to merit further study.

SOME OF THE BEST AND SAFEST INSECTICIDAL MATERIALS have been developed from the study of naturally occurring products. Synergists for pyrethrum fall in this category. From sesame oil Haller, LaForge and Sullivan (*6*) isolated sesamin, a compound found to be strongly synergistic with pyrethins. By examination of compounds similar to sesamin, the 3,4-methylenedioxyphenyl group was shown to be necessary for sesamin's activity.

The fundamental work of Haller and his associates triggered the search for synthetic synergists that could be prepared cheaply enough to be of commercial value. The search has led to the production of such excellent pyrethrum synergists as piperonyl butoxide (*14*), sulfoxide (*13*), piperonyl cyclonene (*14*), and *n*-propyl isome (*12*), all of which contain the 3,4-methylenedioxyphenyl group.

Of late the synergist problem has been complicated by the introduction of synthetic pyrethrin-like compounds, such as allethrin, introduced by Schechter, Green, and LaForge (*11*). With this compound and others such as furethrin (*9*), synergists were found to be much

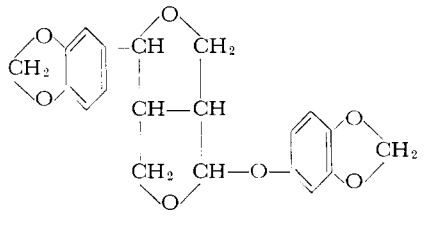
less active than with natural pyrethrins, the degree of synergism not necessarily corresponding to that obtained with natural pyrethrins. More recently cyclethrin, a new synthetic pyrethrin, has been shown to be more synergizable than allethrin (*8*).

After the importance of the 3,4-methylenedioxyphenyl group for synergism had been established, further research on compounds exhibiting synergistic activity was more or less empirical. Compounds were prepared from safrole (or isosafrole), the cheapest source of the 3,4-methylenedioxyphenyl group, and subjected to test. By this procedure there has been little progress in production of new synergists in the last few years.

Recently further investigation of sesame oil was undertaken in an attempt to isolate and identify any constituent other than sesamin that was synergistic with synthetic or natural pyrethrins. The presence of synergism other than that due to sesamin had been recognized by Haller, La Forge, and Sullivan (*6*) as well as by Parkin and Green (*10*). By systematic entomological examination of chromatographic fractions of sesame oil, two pyrethrin synergists, sesamin and sesamolin, were found to account for all the activity of the oil (*2*).

Sesamolin, which had not been known to be synergistic, was found to be about five times as effective as sesamin against the housefly in tests by the turntable method (*5*), an equiproportional mixture of sesamolin and natural pyrethrins increasing the insecticidal value of the latter 31 times. This intense synergism established sesamolin as one of the most potent natural-pyrethrum synergists. Furthermore, this work indicated that the ultimate in synthetic synergists has not yet been attained, inasmuch as sesamolin is far more effective a synergist for natural pyrethrins than the best commercial synergist.

The fact that sesamolin is so potent a synergist made it desirable to elucidate its chemical structure, and on the basis of preliminary evidence the author advanced the following formula (*2*): 2 - (3,4 - methylenedioxyphenoxy) - 6- (3,4 - methylenedioxyphenyl) - 3,7-dioxabicyclo(3.3.0)octane.



Proof of the validity of this formula has recently been reported by the author (*1*) and by two other sources (*4*, *7*). The central nucleus is believed to have a cis configuration, the trans configuration being considered unlikely.

The difference between the formula for sesamin and that given above for sesamolin is that sesamolin contains a 3,4-methylenedioxyphenoxy group in place of one of the 3,4-methylenedioxyphenyl groups of sesamin. In other words, one of the 3,4-methylenedioxyphenyl groups in sesamolin is attached to the rest of the molecule by means of an oxygen, rather than a carbon atom. That this difference should result in such a marked increase in synergism made it desirable to prepare 3,4-methylenedioxyphenoxy derivatives—especially acetals and ethers—as candidate synergists.

The preparation of these compounds represents a fresh approach to the synergist problem, and this paper reports on the preparation of 66 of these compounds, which include, in addition to acetals and ethers, esters, sulfonates, urethans, and some intermediate compounds. All these compounds are new. They have been tested for synergism with pyrethrins and allethrin against the housefly by the turntable method, and some will be studied further. The entomological data will be reported in a later issue of this journal.

Preparation of Compounds

Sesamol The synthesis of sesamol is reported by Boeseken, Cohen, and Kip (*3*). The following is a modification of their directions.

To a stirred solution of 156 grams of 40% peracetic acid [contains 62.5 grams (0.82*M*) of peracetic acid, 8 grams (0.23*M*) of hydrogen peroxide, 20 grams (1.1*M*) of water, 63 grams of acetic acid, and 1.5 grams of sulfuric acid supplied by Becco Chemical Division, Buffalo 7, N. Y.] maintained at 35° to 40° C., add over a 6-hour period a solution containing 136 grams of acetic anhydride (1.33*M*) and 108 grams of acetic acid. The slow addition is necessary to avoid formation of acetyl peroxide, which is explosive. Allow to stand for 16 hours at 25° C, then add 2.8 grams of sodium acetate and 1.6 grams of *p*-toluenesulfonic acid.

Add the resultant solution over a 6-hour period to a stirred solution of 150 grams (1.0*M*) of piperonal in 840 grams of acetic acid maintained at 30° to 35°. After the product has stood for 16 hours at 25°, test for peroxides (starch iodide paper or potassium iodide–sulfuric acid). The test must be absolutely negative even after several minutes before the following distillation is attempted. If the test is positive, add the minimum amount of finely powdered sodium sulfite to get a negative test. The addition of too much sodium sulfite will cause the following distillation to foam.

Distill out the solvents at reduced pressure; then at 5-mm. pressure distill rapidly to a boiling point of 135°. The distillate weighs 136 grams. Discard the 26-gram residue. Mix the distillate (sesamol formate or acetate) with 90 grams (1.6*M*) of potassium hydroxide dissolved in 810 grams of methanol for 2 hours at 25°. Then add 78 grams (1.3*M*) of acetic acid and distill out the solvents at 25 mm. to 65° pot temperature. Take up the oil in 400 grams of ethylene dichloride and wash the solution with 400 ml. of water containing 2 grams of sodium sulfite. Dry over sodium sulfate and distill out the solvents at reduced pressure. Rapidly distill under nitrogen the crude sesamol, boiling point 110–115°/2 mm. Discard the residue (15 grams) and crystallize the crude sesamol (91 grams) from 46 grams of toluene at −15°. Yield is 80 grams (58%), melting point 63°. Store the sesamol in an ice box under nitrogen.

Sesamol Derivatives Many of the following preparations were carried out on a small scale, so that yields better than those reported may be possible. Special studies to obtain maximum yields were not usually made. All melting points are corrected. All elemental determinations but those of nitrogen and chlorine were on a microchemical scale.

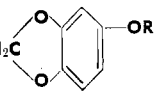
Ethers

The 3,4-methylenedioxyphenyl ethers are shown in Table I. Most of these ethers were prepared according to Method I.

Method I Dissolve 0.02 mole of potassium hydroxide in 95% ethyl alcohol by heating. Cool and add 0.02 mole of sesamol. To this solution add a small excess of the appropriate halide and reflux for several hours or until the potassium halide ceases to form. Take up the product in about 75 ml. of ether, cool, and wash the solution twice with 10- to 20-ml. portions of cold 0.5*N* potassium hydroxide (to remove unreacted sesamol), once with water, and twice with saturated salt solution. Discard all washings. Dry the ether solution over sodium sulfate, filter, evaporate, and distill. In some cases the product crystallized, making unnecessary the distillation or even the wash procedure.

About 65 to 85% yields were obtained by this method, except in syntheses employing secondary halides and alkoxy or polyalkoxy halides, for which the yields were lower. Tertiary halides did not react appreciably. In the case of the alkoxy or polyalkoxy halides higher yields were obtained by Method II.

Method II Dissolve 0.02 mole of sesamol in a 10% methanolic solution of sodium methoxide containing exactly 0.02 mole. To this solution add a small excess of the alkoxy halide, mix, and heat in a sealed tube at 160° for 2 to 3 hours. Take up the product in ether and water and work up as described above.

Table I. 3,4-Methylenedioxyphenyl Ethers 

R	Empirical Formula	Method of Preparation	Yield, %	Boiling Point Temp., °C.	Boiling Point Mm.	M.P., °C.	n_D^{25}	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Propyl	$C_{10}H_{12}O_3$	I	83	67–69	0.08	...	1.5203	66.6	66.98	6.71	6.64
n-Butyl	$C_{11}H_{14}O_3$	I	86	87–88	0.1	...	1.5147	68.0	67.99	7.26	7.17
n-Amyl	$C_{12}H_{16}O_3$	I	84	94–98[a]	0.04–0.07[a]	...	1.5112	69.2	69.28	7.73	7.33
Isoamyl	$C_{12}H_{16}O_3$	I	75	81–84[a]	0.02–0.03[a]	47–48[b]	1.5114[c]	69.2	69.12	7.73	7.36
Cyclopentyl	$C_{12}H_{14}O_3$	I	55	98–101	0.15	...	1.5404	69.9	69.99	6.84	6.79
Cyclohexyl	$C_{13}H_{16}O_3$	II	12.5[d]	104–105	0.08	...	1.5374	70.9	71.22	7.32	7.32
2-*n*-Octyl	$C_{15}H_{22}O_3$	II	51	110–113	0.07	...	1.4996	71.95	71.70	8.86	8.63
2-Ethyl-*n*-hexyl	$C_{15}H_{22}O_3$	I	63	113–116	0.08	...	1.4993	71.95	71.85	8.86	8.68
2-Cyclohexylethyl	$C_{15}H_{20}O_3$	I	78	...	...	56–57[e]	...	72.55	72.64	8.11	7.85
2-*n*-Butoxyethyl	$C_{13}H_{18}O_4$	II	76	117–121	0.085	...	1.5065	62.5	65.54	7.61	7.49
2(2-Chloroethoxy)ethyl	$C_{11}H_{13}O_4Cl$	II[f]	48	131–133	0.07	...	1.5343	54.0	54.65	5.36	5.52
2(2-Ethoxyethoxy)ethyl	$C_{13}H_{18}O_5$	I	22	123–125	0.08	...	1.5107	61.4	60.96	7.12	7.20
2(2-*n*-Butoxyethoxy) ethyl	$C_{15}H_{22}O_5$	II	71	142–145	0.08	...	1.5019	63.7	63.57	7.87	7.62
Allyl	$C_{10}H_{10}O_3$	I	62	84–88	0.1	...	1.5400	67.4	67.36	5.66	5.58
2-Chloroallyl	$C_{10}H_9O_3Cl$	I	75	111–114[a]	0.03–0.04[a]	...	1.5501	56.5	56.72	4.28	4.26
3-Chloroallyl	$C_{10}H_9O_3Cl$	I	62	100–104	0.06	64.5–65.5[f]	1.5578[c]	56.5	56.84	4.28	4.34
Acetic acid	$C_9H_8O_5$	II	78	...	...	155–156[g]	...	55.1	55.29	4.11	4.32
Acetyl chloride	$C_9H_7O_4Cl$	[h]	73	103–104	0.085	67–68[i]	1.5510[c]	[h]	[h]	[h]	[h]
Acetic acid, *n*-butyl ester	$C_{13}H_{16}O_5$	[h]	82	127–131	0.08	...	1.5106	61.9	62.13	6.39	6.48
Trimethyl silyl	$C_{10}H_{14}O_3Si$	[h]	78	124–125	14.5	...	1.4999	57.1	57.22	6.71	6.68
Benzyl	$C_{14}H_{12}O_3$	I	67	125–129[a]	0.02[a]	...	1.5850	73.7	74.08	5.30	5.19
o-Chlorobenzyl	$C_{14}H_{11}O_3Cl$	I	65	...	...	63.7–64.7[f]	...	64.0	63.96	4.23	4.14
p-Chlorobenzyl	$C_{14}H_{11}O_3Cl$	I	64	...	...	82–82.6[f]	...	64.0	63.87	4.23	4.09
2,4-Dichlorobenzyl	$C_{14}H_{10}O_3Cl_2$	I	77	...	...	101.5–103.5[f]	...	56.6	56.61	3.40	3.35
3,4-Dichlorobenzyl	$C_{14}H_{10}O_3Cl_2$	I	80	...	...	68.5–69.3[j]	...	56.6	56.94	3.40	3.45
p-Bromobenzyl	$C_{14}H_{11}O_3Br$	I	61	...	...	92.5–93.5[f]	...	54.75	55.4[k]	3.61	3.69
p-Nitrobenzyl	$C_{14}H_{11}O_5N$	I	...	...	...	119–120[f]	...	61.5	60.75[k]	4.06	3.88
2,2′-Diethyl ether (disesamol ether)	$C_{18}H_{18}O_7$	II	53	...	...	125–126[l]	...	62.4	62.22	5.24	5.29

[a] Temperature of bath and pressure in molecular distillation.
[b] Crystallized from ether–petroleum ether.
[c] Supercooled liquid.
[d] 11.5% yield by method I.
[e] Crystallized from petroleum ether.
[f] Crystallized from ether.
[g] Crystallized from water.
[h] See text for method of preparation.
[i] Not crystallized to constant m.p.
[j] Crystallized from ether-alcohol.
[k] This compound may not be pure.
[l] Crystallized from chloroform-ether.

Other Methods Four ethers given in Table I were prepared by other methods.

2-(2-Chloroethoxy)ethyl 3,4-Methylenedioxyphenyl Ether. Prepare according to Method II, but use 5 moles of halide to 1 of sesamol.

3,4 - Methylenedioxyphenoxyacetyl Chloride. Prepare from the acid by refluxing with excess thionyl chloride in benzene until no more hydrogen chloride is generated (exit tube through kerosine). Remove excess thionyl chloride and benzene under reduced pressure and distill the product. The distillate crystallized after standing overnight and melted at 67–68°. Chlorine found, 16.23%; theory, 16.5%. It was used to prepare the butyl ester without further purification.

Butyl 3,4-Methylenedioxyphenoxyacetate. Treat the acid chloride above with excess butanol and pyridine and allow to remain overnight. Add water, mix well, and after 0.5 hour take up the product in ether and work up as described under Method I.

3,4-Methylenedioxyphenyl Trimethylsilyl Ether. Prepare like an ester from trimethylchlorosilane (in place of acid chloride), pyridine, and sesamol.

Acetals

The acetals are shown in Table II. Those compounds prepared from vinyl ethers were made according to the following procedure.

Destroy any peroxides present in the vinyl ether by treatment with a suitable alkaline reducing agent (sodium sulfite). Distill the vinyl ether to remove any stabilizer (usually di-2-ethylhexylamine). Add a small drop of concentrated hydrochloric acid to 0.025 mole or more of the vinyl ether and, while stirring the solution rapidly (magnetically), add 0.02 mole of sesamol in small portions, allowing each portion to dissolve completely before making the next addition (15 minutes). Heat for 30 minutes at 70° or, if the ether is low boiling, allow to stand for several hours. Add 75 ml. of ether and work up as described under Method I for the preparation of ethers.

2 - Ethoxy - 5 - (3,4 - methylenedioxyphenoxy)tetrahydrofuran. Add a small drop of concentrated hydrochloric acid to 0.02 mole of 2,5-diethoxytetrahydrofuran maintained at 80° while dry nitrogen stirs the solution. Gradually add 0.02 mole of sesamol, then maintain at 80° for 2.5 hours. Cool, add ether, and work up as described under Method I for the preparation of ethers.

Acetaldehyde, 2-(2-Butoxyethoxy)-ethyl 3,4-Methylenedioxyphenyl Acetal. To 1.5 gram of 2-chloroethyl 3,4-methylenedioxyphenyl acetal add 0.2 gram of sodium dissolved in 4 grams of 2-*n*-butoxyethanol. Heat at 160° for 2.5 hours in a sealed tube. Take up the product in ether and water, and work up as described under Method I for the preparation of ethers.

Bis(3,4 - methylenedioxyphenoxy)-methane. Prepare from 0.01 mole of methylene iodide, 0.02 mole of sesamol, and 0.02 mole of potassium hydroxide according to Method I for the preparation of ethers.

Esters and Sulfonates

The data on these compounds are shown in Table III.

Table II. 3,4-Methylenedioxyphenyl Acetals

Derivative[a]	Empirical Formula	Yield, %	Boiling Point Temp., °C.	Boiling Point Mm.	n_D^{25}	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Derivative Prepared from
Acetaldehyde, ethyl R acetal	$C_{11}H_{14}O_4$	90	82–85	0.085	1.5060	62.8	62.64	6.71	6.78	Ethyl vinyl ether
Acetaldehyde, *n*-butyl R acetal	$C_{13}H_{18}O_4$	92	106–110	0.15	1.4970	65.5	65.65	7.61	7.46	*n*-Butyl vinyl ether
Acetaldehyde, isobutyl R acetal	$C_{13}H_{18}O_4$	93	94–97	0.075	1.4964	65.5	65.62	7.61	7.64	Isobutyl vinyl ether
Acetaldehyde, 2-chloroethyl R acetal	$C_{11}H_{13}O_4Cl$	87	111–113	0.08	1.5236	54.0	53.80	5.35	5.19	2-Chloroethyl vinyl ether
Acetaldehyde, 2-*n*-butoxyethyl R acetal	$C_{15}H_{22}O_5$	85	121–125	0.075	1.4930	63.8	63.58	7.85	7.77	2-*n*-Butoxyethyl vinyl ether
Acetaldehyde, 2-methoxyethyl R acetal	$C_{12}H_{16}O_5$	90	107–111	0.09	1.5057	60.0	59.74	6.72	6.56	2-Methoxyethyl vinyl ether
Acetaldehyde, 2-(2-ethoxyethoxy)ethyl R acetal	$C_{15}H_{22}O_6$	89	137–141	0.08	1.4938	60.4	60.35	7.43	7.37	2(2-Ethoxyethoxy)ethyl vinyl ether
Acetaldehyde, 2-ethylhexyl R acetal	$C_{17}H_{26}O_4$	88	120–124	0.075	1.4911	69.4	69.26	8.91	8.86	2-Ethylhexyl vinyl ether
Acetaldehyde, 2-(2-butoxyethoxy)ethyl R acetal	$C_{17}H_{26}O_6$	55	171–175	0.075	1.4908	62.6	62.95	8.03	8.33	2-Chloroethyl R acetal
2-RO-tetrahydropyran	$C_{12}H_{14}O_4$	89	102–107	0.065	1.5347	64.9	65.21	6.35	6.45	Dihydropyran
2-RO-*p*-dioxane	$C_{11}H_{12}O_5$	35	122–125	0.085	1.5411[b]	58.9	58.67	5.395	5.19	*p*-Dioxene
2-Ethoxy-5-RO-tetrahydrofuran	$C_{13}H_{16}O_5$	30	109–115	0.07	1.5190	61.9	62.20	6.40	6.15	2,5-Diethoxytetrahydrofuran
Bis(RO)methane	$C_{15}H_{12}O_6$	44	...	...	[c]	62.5	62.71	4.20	4.28	Methylene iodide

[a] R = 3,4-methylenedioxyphenyl, RO = 3,4-methylenedioxyphenoxy.
[b] Supercooled liquid, m.p. 75.5–76.5°, crystallized from ether.
[c] M.p. 121–122°, crystallized from ether.

Add a slight excess of the appropriate acid chloride to a solution of sesamol in benzene and excess pyridine. Heat the mixture on a steam bath for 15 minutes or allow to remain overnight. Add water, mix well, allow to remain 30 minutes, and work up as described under Method I for the preparation of ethers.

Urethans

The data on the urethans are shown in Table IV.

Heat a mixture of 0.01 mole of sesamol plus a slight excess of the appropriate isocyanate and 2 drops of pyridine for 15 minutes on a steam bath. Crystallize the product from carbon tetrachloride to constant melting point.

Discussion

Every ether of sesamol except the trimethylsilyl derivative (not a C—O—C ether) exhibited synergism, and all the

Table III. 3,4-Methylenedioxyphenyl Esters and Sulfonates

Esters and Sulfonates	Formula	Yield, %	Boiling Point Temp., °C.	Boiling Point Mm.	M.P., °C.	n_D^{25}	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Ester										
Acetate	$C_9H_8O_4$	87	81–3	0.08	...	1.5256	59.95	60.06	4.48	4.54
Propionate	$C_{10}H_{10}O_4$	85	81–3	0.08	...	1.5183	61.8	61.99	5.20	5.15
n-Butyrate	$C_{11}H_{12}O_4$	82	92–4	0.08	...	1.5118	63.4	63.32	5.81	5.68
Caproate	$C_{13}H_{16}O_4$	83	113–7	0.07	...	1.5020	66.1	66.32	6.82	6.62
Palmitate	$C_{23}H_{36}O_4$	81	...	...	50–51[a]	...	73.35	73.68	9.63	9.42
Cyclohexyl carboxylate	$C_{14}H_{16}O_4$	80	125–7	0.08	60–60.5[b]	...	67.7	68.02	6.49	6.46
Furoate	$C_{12}H_8O_5$	90	130–2	0.08	67.8–68.5[c]	...	62.05	62.03	3.47	3.69
Chloroacetate	$C_9H_7O_4Cl$	61[d]	104–6	0.08	54–55[e]	1.5454[f]	50.4	50.63	3.29	3.12
Ethyl carbonate	$C_{10}H_{10}O_5$	75	100–1	0.1–0.2	33.5–34.5[e]	1.5111[f]	57.1	57.31	4.80	4.90
n-Butyl carbonate	$C_{12}H_{14}O_5$	79	107–10	0.07	...	1.5016	60.5	60.60	5.92	5.84
Isobutyl carbonate	$C_{12}H_{14}O_5$	89	106–9	0.07	...	1.5002	60.5	60.58	5.92	5.83
Benzoate	$C_{14}H_{10}O_4$	93	145–8	0.09	56–56.5[c]	1.5879[f]	69.35	69.59	4.16	4.20
o-Ethoxybenzoate	$C_{16}H_{14}O_5$	96	165–70	0.07	62–63[e]	1.5773[f]	67.1	67.18	4.93	4.99
o-Chlorobenzoate	$C_{14}H_9O_4Cl$	86	156–8	0.06	55–56[c]	1.5940[f]	60.8	60.93	3.28	3.52
p-Chlorobenzoate	$C_{14}H_9O_4Cl$	76	...	...	91–92[c]	...	60.8	61.05	3.28	3.57
Chrysanthemumate (synthetic)	$C_{17}H_{20}O_4$	76	120–6	0.05[g]	66–67[c]	...	70.8	71.07	7.01	6.98
Sulfonate										
Benzene sulfonate	$C_{13}H_{10}O_5S$	80	166–70	0.1	62.5–63.5[a]	1.5750[f]	56.1	56.18	3.62	3.61
β-Naphthalenesulfonate	$C_{17}H_{12}O_5S$	76	...	...	89–90[e]	...	62.2	62.19	3.68	3.65
p-Toluenesulfonate[h]	$C_{14}H_{12}O_5S$	85	...	...	86–87[e]	...	57.5	57.80	4.14	4.18
p-Chlorobenzene sulfonate	$C_{13}H_9O_5ClS$	75	...	...	84.5–85.5[e]	...	49.95	50.20	2.90	2.84

[a] Crystallized from ether–petroleum ether.
[b] Crystallized from iso-octane.
[c] Crystallized from benzene–petroleum ether.
[d] Cooled in ice bath on addition of acetyl chloride. If not cooled, yield was only 30%.
[e] Crystallized from ether.
[f] Supercooled liquid.
[g] Molecular still.
[h] Prior synthesis reported (7).

Table IV. 3,4-Methylenedioxyphenyl Urethans

Urethan	Formula	Yield, %	M.P., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
N-Phenyl	$C_{14}H_{11}O_4N$	90	122.0–122.5	C, 65.35 H, 4.32	C, 65.68 H, 4.42
N-*o*-Tolyl	$C_{15}H_{13}O_4N$	87	142.5–143.5	5.16	5.15
N-*m*-Tolyl	$C_{15}H_{13}O_4N$	82	84.5–85.5	5.16	5.12
N-*p*-Tolyl	$C_{15}H_{13}O_4N$	88	152.5–153.5	5.16	5.26
N-1-Naphthyl	$C_{18}H_{13}O_4N$	90	158.0–158.5	4.56	4.56

acetals were strongly synergistic. The carboxylic acid esters showed practically no synergism whereas the sulfonic acid esters were strongly synergistic. Although the urethans were synergistic, the activity was not sufficient to warrant further investigation. Furthermore, the urethans had the disadvantage of being relatively insoluble in kerosine, the most widely used base for insecticides. The compounds that are active are true synergists, as they show no appreciable toxicity in the absence of pyrethrins. Sesamol itself is not appreciably synergistic with pyrethrins (*5*).

The fact that so many of the foregoing compounds having the 3,4-methylenedioxyphenoxy structure exhibited synergism indicates that the premise that this group would give good synergists was correct. The comparison of safrole and the allyl ether of sesamol shows that the latter is much more synergistic. Like sesamin and sesamolin, this is another example where a compound containing the methylenedioxyphenoxy group is superior to the corresponding compound containing a methylenedioxyphenyl group.

Synergism was much greater with the natural pyrethrins than with allethrin. However, the results were generally parallel—that is, a compound synergistic with one was synergistic with the other, although not always to the same degree.

Of all the compounds, the acetals appear to be the most promising candidates for synergists of commercial value. Some of these compounds may be prepared in close to quantitative yield simply by adding sesamol to the vinyl ether plus an acidic catalyst. This reaction is unsatisfactory if the addition is reversed—that is, if the vinyl ether is added to the sesamol plus the catalyst. The acetals are generally soluble in kerosine.

Acknowledgment

The author wishes to express his deep appreciation to the Trubek Laboratories, Inc., East Rutherford, N. J., for supplying much of the sesamol used in this study and for the directions given in this paper for the preparation of sesamol. These directions were used to prepare additional quantities of sesamol needed in this study.

He is also grateful to the Carbide and Carbon Chemicals Co., New York, N. Y., for supplying some of the vinyl ethers used in this study.

Literature Cited

(1) Beroza, M., *J. Am. Chem. Soc.* **77,** 3332 (1955).
(2) Beroza, M., *J. Am. Oil Chemists' Soc.* **31,** 302 (1954).
(3) Boeseken, J., Cohen, W. D., and Kip, C. J., *Rec. trav. chim.* **55,** 815 (1936).
(4) Erdtman, H., and Pelchowicz, Z., *Chemistry and Industry* **1955,** 567.
(5) Gersdorff, W. A., Mitlin, N., and Beroza, M., *J. Econ. Entomol.* **47,** 839 (1954).
(6) Haller, H. L., LaForge, F. B., and Sullivan, W. N., *J. Org. Chem.* **7,** 185 (1942).
(7) Haslam, E., and Haworth, R. D., *J. Chem. Soc.* **1955,** 827.
(8) Haynes, H. L., Guest, H. R., Stansbury, H. A., Sousa, A. A., and Borash, A. J., *Contrib. Boyce Thompson Inst.* **18** (1), 1 (1954).
(9) Matsui, M., LaForge, F. B., Green, N., and Schechter, M. S., *J. Am. Chem. Soc.* **74,** 2181 (1952).
(10) Parkin, E. A., and Green, A. A., *Nature* **154,** 16 (1944).
(11) Schechter, M. S., Green, N., and LaForge, F. B., *J. Am. Chem. Soc.* **71,** 3165 (1949).
(12) Synerholm, M. E., and Hartzell, A., *Contrib. Boyce Thompson Inst.* **14,** 79 (1945).
(13) Synerholm, M. E., Hartzell, A., and Cullmann, V., *Ibid.*, **15,** 35 (1947).
(14) Wachs, H., *Science* **105,** 530 (1947).

Received for review July 16, 1955. Accepted October 29, 1955. Division of Agricultural and Food Chemistry, Pesticides Subdivision, 128th Meeting, ACS, Minneapolis, Minn., September 1955.

INSECTICIDE SYNERGISTS

Determination of Methylenedioxyphenyl-Containing Synergists Used in Analysis of Fly Sprays

MORTON BEROZA

Entomology Research Branch, Agricultural Research Service, U. S. Department of Agriculture, Beltsville, Md.

The chromotropic-sulfuric acid method for the determination of methylenedioxyl groups has been applied to the determination of pyrethrum synergists containing these groups. The utility of the method has been demonstrated by its application to the estimation of piperonyl butoxide, sulfoxide, piperonyl cyclonene, and *n*-propyl isome in fly sprays. The method may also be applicable to the determination of the synergists in aerosol formulations, and means of overcoming interferences encountered with several of the more important constituents are given.

IMPORTANCE OF THE METHYLENEDIOXYPHENYL GROUP in contributing toward synergism with pyrethrins was first recognized by Haller and his coworkers (*6*). Since their fundamental discovery, a number of excellent synergists containing this group (*10–12*) have been produced commercially.

Three methods for the determination of methylenedioxyphenyl-containing synergists have been reported. One is for piperonyl butoxide (*7*), but it is not applicable to other methylenedioxyphenyl synergists. The writer (*1*) has described a general method for the