sealed and heated for 6 hr. at 100°. The mixture was evaporated to dryness and the solid obtained was treated with 50 ml. of cold acetonitrile. Filtration afforded 3 g. (23% conversion) of *N-methylsuccinamide*, m.p. 154–156°, and evaporation of the filtrate yielded unreacted *N*-methylsuccinimide. Recrystallization of the product from acetonitrile raised the melting point to 160–161° (lit. value,[11] m.p. 158–162°).

A mixed melting point between this compound and the higher melting product obtained by the hydrogenolysis of compound VIa gave no depression. The infrared spectra of these two substances were superimposable and showed strong characteristic amide bands at 3.08, 3.21, and 6.10 μ.

Anal. Calcd. for $C_5H_{10}O_2N_2$: C, 46.16; H, 7.75; N, 21.53. Found: C, 46.15; H, 7.83; N, 21.46.

N-Ethoxymethylsuccinamide (IX). In a combustion tube were placed 12.5 g. (0.079 mole) of *N*-ethoxymethylsuccinimide[6] and 50 ml. of 95% ethanol. After saturating the solution with liquid ammonia, the tube was sealed and heated for 6 hr. at 100°. Subsequent evaporation of the solvent afforded a mixture of solid product and liquid starting material which was separated by filtration. Recrystallization of the solid from acetonitrile afforded 6.5 g. (47% conversion) of *N-ethoxymethylsuccinamide*, m.p. 138–145°. Two additional recrystallizations raised the melting point to 146–146.5°.

A mixed melting point determination between this compound and the lower melting product obtained from the reduction of compound VIa showed no depression (m.p. 144–146°). The infrared spectra of these two substances were superimposable and showed strong characteristic amide bands at 2.95, 3.01, 3.12 and 6.08 μ and an aliphatic ether band at 9.05 μ.

Anal. Calcd. for $C_7H_{14}O_3N_2$: C, 48.26; H, 8.10; N, 16.08. Found: C, 48.17; H, 8.09; N, 16.34.

LAFAYETTE, INDIANA

(11) F. S. Spring and J. C. Woods, *J. Chem. Soc.*, 628 (1945).

[CONTRIBUTION FROM THE ENTOMOLOGY RESEARCH DIVISION, AGRICULTURAL RESEARCH SERVICE, U. S. DEPARTMENT OF AGRICULTURE]

Synthesis of Methylenedioxyphenyl Compounds from Isosafrole and Sesamol

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During a search for compounds with improved insecticidal activity, 31 new ethers and esters were synthesized from sesamol and isosafrole. Methods of preparation, physical constants, and some biological information are reported herein.

As part of our search for new compounds with improved insecticidal activity, 3,4-methylenedioxyphenyl compounds containing a halogen in the 6- position of the phenyl group were synthesized. Their preparation and that of their intermediates, totaling 31 new compounds, are given. Most were obtained in good or high yield.

Some of the compounds are related to the insecticide 6-chloropiperonyl chrysanthemumate (barthrin)[1]; *i.e.*, they contain a bromine instead of a chlorine atom in the 6- position of the 3,4-methylenedioxyphenyl group. Unfortunately, no substantial improvement in insecticidal activity over barthrin was attained. The addition of bromine usually increased insecticidal activity over the unbrominated analog, but it also decreased activity in several instances.

The derivatives of isosafrole (1,2-methylenedioxy-4-propenylbenzene), given in Table I, were prepared essentially as outlined by Pond and coworkers[2] with one improvement. These investigators brominated isosafrole in ether and reported no yields; we used both ether and glacial acetic acid as solvents and obtained higher yields and a purer product with the latter.

Derivatives of sesamol (3,4-methylenedioxyphenol), given in Table II, were prepared according to published procedures.[3] The shift of the double bond (conversion of an allyl to a propenyl group) and the preparation of allylmethylenedioxyphenol from its ether precursor, by the Claisen rearrangement, were carried out in the usual way.[4] Bromination of the double bond took place readily in a solution of glacial acetic acid at 10°.

Results of screening the compounds as chigger and body louse toxicants, mosquito larvicides, and mosquito repellents are given in Table III. The methods of test and classification of activity are the same as those given by King.[5a] Some of the ethers (I–X) of Table I showed excellent activity as mosquito larvicides; however, the corresponding activity of the esters (XI–XVIII) was nil. Good larvicidal and pediculocidal activities were shown by the sesamol ethers (XX–XXVI); one of these (XX) is a positional isomer of myristicin (3,4-methylenedioxy-5-methoxy-1-allylbenzene), a natural product known to be synergistic with pyrethrins.[6] The best pediculocide (XXIII) differs

(1) W. F. Barthel and B. H. Alexander, *J. Org. Chem.*, **23**, 1012 (1958); W. A. Gersdorff and P. G. Piquett, *J. Econ. Entomol.*, **62**, 85 (1959).

(2) F. J. Pond, E. S. Erb, and A. G. Ford, *J. Am. Chem. Soc.*, **24**, 327 (1902); F. J. Pond and C. R. Siegfried, *J. Am. Chem. Soc.*, **25**, 262 (1903).

(3) L. Claisen and O. Eisleb, *Ann.*, **401**, 36 (1913); C. F. H. Allen and J. W. Gates, Jr., *Org. Syntheses*, **Coll. Vol. III**, 140 (1955).

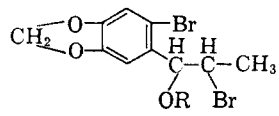
(4) D. S. Tarbell, *Org. Reactions*, **2**, 26 (1944).

(5a) W. V. King, *U. S. Dept. Agr. Handbook*, No. 69, 397 pp. (1954). (b) p. 2.

(6) R. Kerr, Australia, *Commonwealth Sci. and Ind. Res. Bull.* **261** (1951).

TABLE I

ETHERS FROM 1,2-DIBROMO-1-(2-BROMO-4,5-METHYLENEDIOXYPHENYL)PROPANE AND ESTERS FROM 6-BROMO-*alpha*-(1-BROMOETHYL)PIPERONYL ALCOHOL



No.	R	Yield, %	B.P./ (Mm.)	n_D^{25} or M.P.	Molecular Formula	Analysis			
						Carbon		Hydrogen	
						Calcd.	Found	Calcd.	Found
I	C_3H_7	82	125–127/0.03	1.5587	$C_{13}H_{16}Br_2O_3$	41.07	41.11	4.21	4.37
II	C_4H_9	85	138–140/0.05	1.5536	$C_{14}H_{18}Br_2O_3$	42.64	42.57	4.57	4.46
III	C_5H_{11}	78	146–148/0.03	1.5488	$C_{15}H_{20}Br_2O_3$	44.12	44.40	4.90	5.39
IV	$CH_2(CH_2)_4CH_3$	86	150–152/0.03	1.5449	$C_{16}H_{22}Br_2O_3$	45.50	45.61	5.21	4.87
V	$CH_2CH_2OCH_3$	62	153–154/0.05	1.5659	$C_{13}H_{16}Br_2O_4$	39.39	39.74	4.04	4.31
VI	$CH_2CH_2OC_2H_5$	75	147–149/0.03	1.5577	$C_{14}H_{18}Br_2O_4$	40.97	41.10	4.39	4.27
VII	$CH_2CH_2OC_4H_9$	68	163–164/0.03	1.5467	$C_{16}H_{22}Br_2O_4$	43.84	42.73[a]	5.02	5.17
VIII	$CH(CH_3)_2$	79		58–59 (alcohol)	$C_{13}H_{16}Br_2O_3$	41.07	39.47[a]	4.21	5.06
IX	$CH_2CH(CH_3)_2$	87	137–138/0.04	1.5547	$C_{14}H_{18}Br_2O_3$	42.64	42.08	4.57	4.96
X	$CH_2CH_2CH(CH_3)_2$	92	141–142/0.03	1.5487	$C_{15}H_{20}Br_2O_3$	44.12	43.54	4.90	5.09
XI	$\overset{O}{\overset{\|}{C}}—CH_2Cl$	61	180/0.6	1.5808	$C_{12}H_{11}Br_2ClO_4$	34.74	34.96	2.65	2.89
XII	$\overset{O}{\overset{\|}{C}}—CH(CH_3)_2$	66	162/0.1	1.5608	$C_{14}H_{16}Br_2O_4$	41.17	41.17	3.92	4.02
XIII	$\overset{O}{\overset{\|}{C}}—C_2H_5$	90	162–175/0.7	1.5683	$C_{13}H_{14}Br_2O_4$	39.62	40.16	3.58	3.72
XIV	$\overset{O}{\overset{\|}{C}}—C_{10}H_7$	80		130–132 (benzene and methanol)	$C_{21}H_{16}Br_2O_4$	51.24	51.34	3.28	3.49
XV	$\overset{O}{\overset{\|}{C}}—C_6H_4Cl$	87		93–94 (alcohol)	$C_{17}H_{13}Br_2ClO_4$	42.84	43.09	2.75	2.97
XVI	$\overset{O}{\overset{\|}{C}}—C_4H_3O$	88		111–112 (methanol and water)	$C_{15}H_{12}Br_2O_5$	41.69	41.92	2.80	3.12
XVII	$\overset{O}{\overset{\|}{C}}—CCl_3$	83		103–105 (alcohol)	$C_{12}H_9Br_2Cl_3O_4$	29.81	29.77	1.88	2.09
XVIII	$\overset{O}{\overset{\|}{C}}—C_6H_4OCH_3$	87		118–119 (alcohol)	$C_{18}H_{16}Br_2O_5$	45.79	45.30	3.42	3.44

[a] The low values are probably due to some impurity which we were not able to remove.

from the other sesamol ethers in that it contains a triple bond.

The striking feature of Table III is the variation in effectiveness shown by the compounds against different species of arthropods. As in the King report,[5b] the results indicate that compounds ineffective against one species may be effective against another.

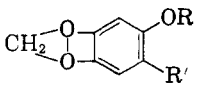
Several of the compounds were not subjected to all the entomological tests because of insolubility in solvents, obnoxious odor, toxicity to warm-blooded animals, or skin irritation.

EXPERIMENTAL

The physical properties, yields, and elemental analyses of the individual compounds are given in Tables I and II.

TABLE II

COMPOUNDS DERIVED FROM SESAMOL (3,4-METHYLENEDIOXYPHENOL)



No.	R	R′	Yield, %	B.P./ (Mm.)	n_D^{25} or M.P.	Molecular Formula	Analysis			
							Carbon		Hydrogen	
							Calcd.	Found	Calcd.	Found
XIX	H	$CH_2CH{:}CH_2$	77	122–128/ 1.3	76–77 (benzene[a])	$C_{10}H_{10}O_3$	67.40	67.80	5.66	5.97
XX	CH_3	$CH_2CH{:}CH_2$	63	119–124/ 2.5	1.5412	$C_{11}H_{12}O_3$	68.73	68.84	6.30	6.44
XXI	C_3H_7	$CH_2CH{:}CH_2$	51	108–114/ 0.4	1.5268	$C_{13}H_{16}O_3$	70.88	69.91	7.32	7.18
XXII	$CH_2C(CH_3){:}CH_2$	H	63	100–101/ 0.9	1.5324	$C_{11}H_{12}O_3$	68.73	68.17	6.30	6.17
XXIII	$CH_2C{:}CH$	$CH_2CH{:}CH_2$	73	113–121/ 0.5	1.5482	$C_{13}H_{12}O_3$	72.20	72.08	5.60	5.54
XXIV	$CH(CH_3)_2$	$CH_2CH{:}CH_2$	45	98–100/ 0.2	1.5242	$C_{13}H_{16}O_3$	70.88	71.44	7.32	7.33
XXV	C_3H_7	C_3H_7	79	157–162/ 18	1.5119	$C_{13}H_{18}O_3$	70.24	69.73	8.16	8.01
XXVI	CH_3	$CH_2C(CH_3){:}CH_2$	74	93–110/ 0.6	1.5510	$C_{12}H_{14}O_3$	69.88	69.31	6.84	6.58
XXVII	O ‖ C—C_9H_{15}	$CH_2C(CH_3){:}CH_2$	44	133–160/ 1.0	1.4968	$C_{21}H_{26}O_4$	73.66	73.96	7.65	7.85
XXVIII	CH_3	$CH{:}CHCH_3$	37		48–49 (alcohol)	$C_{11}H_{12}O_3$	68.73	68.97	6.30	6.23
XXIX	$CH_2CHBrCH_2Br$	Br	80		67–68 (methanol)	$C_{10}H_9Br_3O_3$	28.81	28.96	2.18	2.45
XXX	CH_3	$CH_2CHBrCH_2Br$	46		121–122 (methanol and acetone)	$C_{11}H_{12}Br_2O_3$	37.53	37.94	3.44	3.61
XXXI	C_2H_5	$CH_2CHBrCH_2Br$	64		70–71 (methanol)	$C_{12}H_{14}Br_2O_3$	39.37	39.53	3.86	3.95

[a] Product quite soluble in benzene.

1,2-Dibromo-1-(2-bromo-4,5-methylenedioxyphenyl)propane. A mixture of isosafrole (324 g.) and glacial acetic acid (700 ml.) was cooled to 0° in a 4 l. beaker, and a solution of bromine (640 g.) in glacial acetic acid (400 ml.) was added dropwise with stirring over a period of 2 hr., while the temperature was kept below 15°. Crystallization occurred, and the mixture was allowed to stand at 25° overnight. After filtering off and washing the crystals with normal pentane and then water, a crude product melting at 101–106° (lit. 110–111°[2]) was obtained in 76% yield. Recrystallization from acetone and ether produced a pure product; however, the crude material was pure enough for use as an intermediate.

Ethers prepared from 1,2-dibromo-1-(2-bromo-4,5-methylenedioxyphenyl)propane (Table I, I–X). The preparation of 4-bromo-5-[2-bromo-1-(2-ethoxyethoxy)propyl]-1,2-methylenedioxybenzene (VI) illustrates the procedure. 1,2-Dibromo-1-(2-bromo-4,5-methylenedioxyphenyl)propane (40 g.) was mixed with redistilled 2-ethoxyethanol (100 ml.) and heated gently under reflux for several hours. The excess 2-ethoxyethanol was removed by distillation and the residue distilled *in vacuo*.

Esters prepared from 6-bromo-α-(1-bromoethyl)piperonyl alcohol (Table I, XI–XVIII). The preparation of 6-bromo-α-(1-bromoethyl)piperonyl ester of 1-naphthoic acid (XIV) is typical. 6-Bromo-α-(1-bromoethyl)piperonyl alcohol[2] (34 g.), dry benzene (300 ml.), and pyridine (10 ml.) were mixed and 1-naphthoyl chloride (19.4 g.) was added with stirring. The mixture was heated gently at 40° for 6 hr. and allowed to stand at 25° overnight. The product was poured into a separatory funnel containing water, and the separated benzene layer was washed with 5% aqueous hydrochloric acid, water, saturated sodium bicarbonate, and finally with a saturated salt solution. The benzene layer was dried over anhydrous sodium sulfate, filtered, and after removal of the benzene a crystalline product was obtained. The noncrystalline esters were distilled for final purification.

2-Allyl-4,5-methylenedioxyphenol (Table II, XIX) *and related phenols.* The preparation of XIX is typical. 3,4-Methylenedioxyphenyl allyl ether[7] (89 g.) was heated under reflux in a stream of nitrogen to 220°, at which point the heating bath was removed and a very vigorous reaction (can get violent) took place raising the liquid temperature rapidly to 270°. When the temperature had fallen to 210°, heating with the bath was resumed for 0.5 hr. keeping the temperature at 210–220°. Distillation *in vacuo* gave the desired product.

(7) M. Beroza, *J. Agr. Food Chem.*, **4**, 49 (1956).

TABLE III

RESULTS OF BIOLOGICAL TESTS WITH COMPOUNDS IN TABLES I AND II AGAINST VARIOUS ARTHROPODS[a]

No.	Chigger[b] Toxicant	Body Louse[c] Toxicant	Mosquito[d] Larvicide	Mosquito[e] Repellent
I	1	1	1	1
II	1	1	4	1
III	1	1	4	1
IV	1	1	2	1
V	1	1	2	1
VI	1	1	3	1
VII	1	2	4	1
VIII	1	1	4	1
IX	1	1	4	1
X	1	1	4	1
XI	1	1	1	1
XII	1	1	1	1
XIII	2	1	1	1
XIV	1	2	1	1
XV	1	1	1	1
XVI	1	1	1	...
XVII	...	3	1	...
XVIII	1	1	1	...
XIX	3	1	1	2
XX	...	3	2	1
XXI	...	4	3	1
XXII	...	3	3	1
XXIII	...	4A	3	1
XXIV	...	3	3	1
XXV	...	4	3	1
XXVI	...	4	3	1
XXVII	...	1	1	1
XXVIII	...	...	...	...
XXIX	1	1	2	1
XXX	...	1	1	1
XXXI	...	1	1	1

[a] Classification same as that given by King,[5a] class 1 least and class 4 or 4A most effective. [b] *Trombicula splendens* Ewing. [c] *Pediculus humanus humanus* L. [d] *Anopheles quadrimaculatus* Say. [e] *Aedes aegypti* (L.).

Ethers and esters (Table II, XX–XXI, XXIII–XXXI) *from phenols.* The ethers were prepared from the phenol, alkyl bromide, potassium carbonate, and dry acetone according to published procedures.[3] The ester was prepared in the usual way from a mixture of the phenol, benzene, pyridine, and the acid chloride.

1,2-Methylenedioxy-5-methoxy-4-propenylbenzene (Table II, XXVIII). XX (64 g.) was dissolved in 150 ml. of a saturated solution of potassium hydroxide in methanol.[4] Methanol was removed by distillation until a liquid temperature of 110° was reached, and the solution was then refluxed for 6 hr. After cooling, the mixture was poured into cold water and extracted with ether. The ether layer was washed with a saturated salt solution and dried over anhydrous sodium sulfate. After filtering and evaporating the ether, the residue (XXVIII) crystallized.

5-Bromo-1,2-methylenedioxy-4-(2,3-dibromopropoxy)-benzene (XXIX). A mixture of 3,4-methylenedioxyphenyl allyl ether[7] (47 g.) and glacial acetic acid (200 ml.) was cooled to 0°, and bromine (86 g.) was added with stirring at such a rate as to maintain the temperature below 15°. Stirring was continued for an additional hour at 15° and the mixture was allowed to stand at 25° overnight, after which it was poured into ice and water with stirring. After several hours the supernatant was decanted from the dark residue, and the latter was washed twice with cold water. Cold water was again added to the residue, and it was scratched to produce crystallization. The crystals were filtered, washed with cold water, and dried.

4-(2,3-Dibromopropyl)-5-methoxy-1,2-methylenedioxybenzene (XXX). This compound was prepared as above from XX (0.2 mole) and bromine (0.2 mole). The corresponding ethoxy compound (XXXI) was prepared from the ethoxy derivative in the same manner.

Acknowledgment. We are grateful to Shulton Inc., Clifton, N. J., for the sesamol used in this study, and to Dr. Carroll N. Smith and others of the staff of the Orlando, Fla., laboratory of the Entomology Research Division for conducting the biological tests.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF FLORIDA]

Ocimene

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This paper describes an improved apparatus for preparing ocimene from α-pinene. It also outlines the method of analysis of the product mixture. Infrared absorption curves of ocimene, alloöcimene, dipentene, α-pinene, alloöcimene dimer, and a synthetic mixture of the products are included. The values calculated for ocimene were n_D^{25} 1.4851, d^{25} 0.7926 g./cc.

In 1907, Enklaar[1] stated that he obtained some ocimene by the isomerization of alloöcimene under the influence of a mixture of sulfuric and acetic acids. The known behavior of ocimene and alloöcimene makes such an isomerization unlikely. Several attempts in this laboratory to verify Enklaar's statement were unsuccessful.

In 1940, Rice[2] reported the vapor phase formation of ocimene from α-pinene. In 1951, Hawkins and Hunt[3] published a description and method of operating an apparatus for the production of ocimene from α-pinene in the vapor phase. More recently O'Connor and Goldblatt[4] indicated that they have prepared ocimene by the isomerization

(1) C. J. Enklaar, *Rec. trav. chim.*, **26**, 157 (1907).
(2) F. O. Rice, U. S. Patent **2,190,369**, Feb. 13, 1940.
(3) J. E. Hawkins and H. G. Hunt, *J. Am. Chem. Soc.*, **73**, 5379 (1951).
(4) R. T. O'Connor and L. A. Goldblatt, *Anal. Chem.*, **26**, 1726 (1954).