tities might be expected to favor the "organic" reductive route rather than the hydroxylation characteristic of the aqueous system. The reduction process appears to occur by a radical pathway since radical recombination products such as the Photo-Fries product, and nonan-5-one, (2-oxopropyl)-2-pentenoate, and the expected Norrish Type II product (the free acid) were detected. The presence of the Photo-Fries product in the formulation study but not in the irradiation of the pure ester implies that the mixed micelles must constitute fairly "tight" radical cages to allow the Photo-Fries to occur (Kelly et al., 1969). This is further evidence for the existence of micellar aggregates.

In addition, the results indicate that the photoproducts expected from sprayed mixed ester emulsion concentrates should be the same whether or not the water carrier evaporates from the impinged droplets.

The major photoproduct, the ester of (*p*-chlorophenoxy)acetic acid, is much more volatile than the parent ester, since its retention time on the same GC column is about half that of the parent ester. As the chlorophenoxyacetate is still quite phytotoxic (Thompson et al., 1946), this could pose a possible threat to nontarget plants. This threat would not be appreciably diminished by use of such "nonvolatile" active ingredients as the isooctyl or butoxyethanol esters since, on dechlorination, volatile phytotoxic photoproducts would also be produced. To minimize environmental pollution from this source, amine salt formulations should be used whenever possible (Que Hee and Sutherland, 1974b).

An interesting effect is demonstrated by the difference in decomposition rates observed in Pyrex and quartz vessels. Although photodegradation was negligible at 350 nm, it was quite appreciable at 300 nm using Pyrex vessels to produce nearly 40% conversion for the pure *n*-butyl ester in 8 h. This situation simulates the sunlight photolysis of sprayed droplets from which all the water carrier has been evaporated so that the 2,4-D ester is in an excess of volatile "inert" components.

This study is one of the first published on the photochemistry of a commercially produced formulation for which the constituent chemicals have been stated and for which a complete mass balance with respect to the active ingredient (in this case the free acid) has been demonstrated by utilizing ^{14}C radiolabel at all its carbon atoms.

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1-[(5,9-Dimethyl-3,8-decadienyl)oxy]benzene and Derivatives: Vinylogues of Aryl Citronellyl Ethers Highly Effective as Juvenile Hormone Mimics

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Twenty-two 5,9-dimethyl-3,8-decadienyl aryl ethers and the corresponding 8,9-epoxy, 9-methoxy, and 9-ethoxy analogues were synthesized as well as eight 6,10-dimethyl-4,9-undecadienyl aryl ethers plus the corresponding 9,10-epoxy analogues. Bioassay data on the large milkweed bug (*Oncopeltus fasciatus*) and the yellow mealworm (*Tenebrio molitor*) are given. Most of the epoxide derivatives showed outstanding activity against *O. fasciatus*, and the meta-substituted derivatives were generally much more active than the corresponding para-substituted isomers. The *Z* configuration of the disubstituted double bond at the 3-position of the side chain is not detrimental to exceptional activity. The *Z* isomer generally showed a substantial increase in biological activity against both *O. fasciatus* and *T. molitor* over that of the *E* isomers in the comparisons made. In no case was the *E* isomer more active than the *Z* isomer.

Over the past decade, numerous chemicals exhibiting juvenile hormone (JH) activity against a variety of insects were discovered and are described in the literature. Several review articles adequately cover much of this work (Menn and Beroza, 1972; Slama et al., 1974; Henrick et al., 1976).

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One particular group of chemicals that has received extensive investigation is the aryl terpenoid type of JH mimic. Most of these chemicals were aryl terpenoid ethers, amines, carbamates, or hydrocarbons derived from the appropriate geranyl, "ethylgeranyl" (3,7-dimethyl-2,6-nonadienyl), citronellyl, or farnesyl moiety. While much work has been reported on changes in biological activity associated with the aryl substitution, derivatization of the 6,7 (or terminal) double bond of the terpenoid arm, and manipulations with the methyl branches on the side chain, relatively little information has been reported on biological effects associated with terpenoid side chains other than

the geranyl, "ethylgeranyl", citronellyl, or farnesyl moieties (Schwarz et al., 1971; Ozawa et al., 1974).

We have been interested in relationships between the chemical structure of aryl terpenoid ethers and their biological activity for some time. Our most recent investigations were concerned with biological activity associated with various extensions of the terpenoid side chain. We report here the synthesis and biological activity of 5,9-dimethyl-3,8-decadienyl aryl ethers and their 8,9-epoxy, 9-methoxy, and 9-ethoxy analogues in tests against the large milkweed bug, *Oncopeltus fasciatus*, and the yellow mealworm, *Tenebrio molitor*.

EXPERIMENTAL PROCEDURES

General. Gas chromatography (GC) was conducted on a Varian 2740 instrument equipped with a flame ionization detector. A 5 ft × $^1/_8$ in., 3% G.C. SE 30 on 100/120 mesh Varaport 30 column was used for all analyses except for the epoxides, for which a 16 in. × $^1/_8$ in. column packed with the same support was used. Injection port and detector temperatures were 275 and 285 °C, respectively. Column temperature was optimized as needed. Nitrogen was the carrier gas. Infrared spectra were obtained on a Perkin Elmer 457A grating spectrophotometer as films between salt plates. Proton magnetic resonance spectra (^{1}H NMR) were run in carbon tetrachloride on a Varian T60 instrument with tetramethylsilane (Me_4Si) as the internal standard. GC–mass spectra (electron impact) were determined with a Finnigan Model 4000 instrument (with a Model 6000 data system) equipped with a glass open tubular column (GOTC); SP2100 GOTC, 30 m × 0.25 mm (i.d.). The mass spectra were recorded at 70-eV ionization potential and a source temperature of 250 °C. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

General Synthesis Procedure. The aryl alkadienyl ethers were prepared via the Wittig coupling of the appropriate substituted 3-phenoxypropylidenetriphenylphosphorane or 4-phenoxybutylidenetriphenylphosphorane and 2,6-dimethyl-5-heptenal in dimethyl sulfoxide. [The substituted phenoxyalkyl bromides were prepared by the method of Marvel and Tanenbaum (1941).] Butyllithium was used as a base in the formation of the phosphorane. Isolation was accomplished by extraction into hexane after pouring the reaction mixture into ice–water. The organic layer was dried over anhydrous magnesium sulfate. After removal of the solvent, the crude product was distilled under vacuum to provide an average yield of 60–70%. A portion of the distilled product was purified further for the bioassay test by column chromatography on Florisil. Hexane and 1% and 2% ether–hexane were used sequentially as eluants. Olefins prepared in a manner similar to this procedure were predominantly in the *Z* form (Corey and Kwiatkowski, 1966; Kovaleva et al., 1974). GC separation with the capillary system and mass spectral data confirmed the geometry of the olefins from these syntheses as >90% *Z* isomer. The *E* isomer content usually varied from 5 to 7%. The *E* isomers were prepared by the method of Anderson and Henrick (1975). When the Wittig reaction was carried out in anhydrous ether at −70 °C and methanol was used to facilitate equilibration of the Wittig intermediate adduct a *Z,E* isomer mixture whose composition was >60% *E* was obtained. The *E* isomer was obtained by column chromatography with silver nitrate impregnated silica gel. Hexane was used as the eluant.

The 8,9- and 9,10-epoxides were prepared via the standard procedure of epoxidation of the dienyl precursor with *m*-chloroperbenzoic acid in methylene chloride at 0–5 °C. Purification was accomplished by column chromatography on Florisil with hexane and 2, 5, and 10% ether–hexane as sequential eluants.

The 9-alkoxy derivatives were prepared by alkoxymercuration of the aryl alkadienyl ethers in methanol or ethanol, followed by demercuration with sodium borohydride (Brown and Rei, 1969). The crude products were purified in the same manner as were the epoxides.

The structures of the 5,9-dimethyl-3,8-decadienyl aryl ethers were confirmed by elemental and spectroscopic analyses. The *m/e* mass spectral peaks for the molecular ions (M^+) were consistent with the molecular weights of the assigned structures. The structures of the 8,9-epoxy and 9-alkoxy analogues were confirmed by mode of synthesis and spectral analysis.

The ^{1}H NMR for 1-[(5,9-dimethyl-3,8-decadienyl)-oxy]benzene and its epoxy and alkoxy analogues (compounds **17**, **37**, **53**, and **77** of Table I) are typical (δ scale in parts per million from Me_4Si). **17**: 0.95 (d, 3, J = H_z, C-5 CH_3), 1.57 and 1.67 (2 s, 6, C-9 CH_3), 2.49 (m, 3, H-2 and H-5), 3.90 (t, 2, J = 7 H_z, H-1), 5.05 (m, 1, H-8), 5.35 (m, 2, H-3 and H-4), 7.00 (m, 5, aryl). **37**: 0.98 (d, 3, J = 7 H_z, C-5 CH_3), 1.18 and 1.21 (2 s, 6, C-9 CH_3), 2.52 (m, 4, H-2, H-5, and H-8), 3.90 (t, 2, J = 7 H_z, H-1), 5.37 (m, 2, H-3 and H-4), 7.00 (m, 5, aryl). **53**: 0.98 (d, 3, J = 6 H_z, C-5 CH_3), 1.06 (s, 6, C-9 CH_3), 2.48 (m, 3, H-2 and H-5), 3.08 (s, 3, OCH_3), 3.88 (t, 2, J = 7 H_z, H-1), 5.34 (m, 2, H-3 and H-4), 7.00 (m, 5, aryl). **77**: 0.98 (d, 3, J = 7 H_z, C-5 CH_3), 1.05 and 1.09 (t overlapping a s, J = 7 H_z, 9, $OCH_2\mathbf{CH}_3$ and C-9 CH_3), 2.50 (m, 3, H-2 and H-5), 3.27 (q, 2, J = 7 H_z, $O\mathbf{CH}_2CH_3$), 3.89 (t, 2, J = 7 H_z, H-1), 5.33 (m, 2, H-3 and H-4), 7.00 (m, 5, aryl). All compounds were >95% pure by gas chromatographic analysis and all were racemic compounds.

Bioassay. With *T. molitor*, the compounds were applied topically in acetone solution (1 μL/pupa) to the last three abdominal segments of the ventral side of 2- to 8-h-old pupae, with a calibrated glass disposable micropipet. The treated pupae (five pupae/test) were held in a 9-cm plastic petri dish until they molted normally or morphological changes characteristic of JH activity were noted. The rating system was: 0 = perfect adult; 1 = retention of either gin traps or urogomphi; 2 = retention of both gin traps and urogomphi; 3 = intermediate, retention of gin traps and urogomphi plus retention of pupal cuticle in the area of treatment; 4 = second pupa, retention of all pupal characteristics. With *O. fasciatus*, the compounds were applied topically in acetone solutions (1 μL/nymph) to the last three abdominal segments of the ventral side of 2- to 8-h-old fifth instar nymphs, with a calibrated glass disposable micropipet. The treated nymphs (five nymphs/test) were held in a 0.5-pt ice cream carton capped with a clear plastic petri dish lid (supplied with milkweed seed for food and cotton stoppered water vials) until they molted normally or morphological changes characteristic of JH activity were noted. The rating system was: 0 = perfect adult; 1 = perfect adult, except for retention of nymphal coloration on the abdomen; 2 = adult with reduced wings and nymphal coloration on the abdomen; 3 = supernumerary nymph, the retention of all nymphal characteristics. The compounds were tested at 10 μg/μL levels and, if active, at lower concentrations until an average rating of 1.0 for *O. fasciatus* and *T. molitor* was obtained.

RESULTS AND DISCUSSION

Table I gives results of the bioassay. The chemicals are grouped in four sections and are listed in decreasing order in each section according to their ability to cause maximum

Table I. Juvenile Hormone Activity of Vinylogues of Citronellyl Aryl Ethers

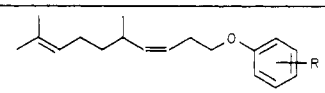
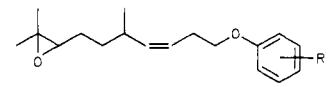
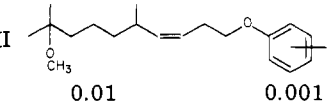
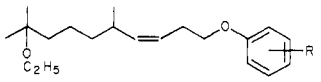
		dosage (μg) causing juvenilization ratings of[a]			
		O. fasciatus		*T. molitor*	
no.	R	3.0	⩾1	4.0	⩾1
	I 				
1	3,4-OCH_2O[b]	0.01	0.001	1	0.1
2	4-OC_2H_5[b]	0.01	0.01		10
3	3-OCH_3[b]	0.01	0.01	10	1
4	3-F[b]	0.1	0.01		10
5	3-OC_2H_5[b]	0.1	0.01		10
6	3-Cl	0.1	0.1		10
7	4-F	0.1	0.1		10
8	3-C_2H_5	0.1	0.1	1	1
9	4-C_3H_7	0.1	0.1		10
10	4-Br	1	0.1		10
11	4-C_2H_5	1	0.1	1	0.1
12	4-$CH(CH_3)_2$	1	0.1		10
13	4-OCH_3	1	0.1	10	10
14	3-CH_3	1	0.1		10
15	4-CH_3	1	0.1		1
16	3,4-Cl_2	1	0.1		10
17	H	1	0.1	10	10
18	3,4-$(CH_3)_2$	1	0.1		10
19	4-Cl	1	1		10
20	3-CF_3	10	0.1		c
21	3,5-$(CH_3)_2$	10	1		10
22	4-$C(CH_3)_3$		10		c
	II 				
23	3-Cl[b]	0.001	0.0001		10
24	3-C_2H_5[b]	0.001	0.0001		10
25	3-OCH_3[b]	0.001	0.001		1
26	3-OC_2H_5[b]	0.001	0.001		10
27	3-F[b]	0.001	0.001		10
28	4-F[b]	0.001	0.001		10
29	3,4-OCH_2O[b]	0.01	0.001	1	0.1
30	3,4-Cl_2	0.01	0.001		10
31	4-Cl[b]	0.1	0.01		1
32	4-C_2H_5[b]	0.1	0.01	0.1	0.01
33	4-Br	0.1	0.01		1
34	4-OC_2H_5	0.1	0.01		1
35	3-CH_3	0.1	0.01		1
36	3-CF_3	0.1	0.01		c
37	H	0.1	0.01	10	10
38	3,4-$(CH_3)_2$	0.1	0.01		1
39	4-C_3H_7	0.1	0.01	10	1
40	3,5-$(CH_3)_2$	0.1	0.1		10
41	4-OCH_3	1	0.1		1
42	4-CH_3	1	0.1	10	1
43	4-$C(CH_3)_3$	10	1		1
44	4-$CH(CH_3)_2$		c		1
	III 				
45	3-OCH_3[b]	0.01	0.001		10
46	3,4-OCH_2O	0.01	0.01	10	0.1
47	3-F	0.1	0.01		10
48	3-Cl	0.1	0.01		c
49	3-CH_3	0.1	0.1		10
50	3,4-Cl_2	0.1	0.1		10
51	3-C_2H_5	0.1	0.1		10
52	4-OCH_3	1	0.1		10
53	H	1	1		10
54	3-OC_2H_5	1	1		c
55	4-CH_3	1	1	10	1
56	4-F	1	1		10
57	4-C_2H_5	1	1	10	0.1
58	4-Br	10	1		1
59	4-OC_2H_5	10	1		1
60	4-C_3H_7	10	1		10
61	4-Cl	10	10		10

Table I (*Continued*)

62	3-CF_3		10		*c*
63	3,5-$(CH_3)_2$		10		*c*
64	4-$CH(CH_3)_2$		10		10
65	3,4-$(CH_3)_2$		*c*		10
66	4-$C(CH_3)_3$		*c*		*c*
	IV 				
67	3-OCH_3[b]	0.01	0.001	10	1
68	3,4-OCH_2O	0.1	0.01	1	0.1
69	3-Cl	0.1	0.01		*c*
70	3-F	0.1	0.01		10
71	3-CH_3	0.1	0.1		10
72	3-C_2H_5	0.1	0.1		10
73	4-OCH_3	1	0.1	10	0.1
74	3,4-Cl_2	1	1		10
75	3-OC_2H_5	1	1		10
76	4-F	1	1	1	0.1
77	H	10	1	10	0.1
78	4-CH_3	10	1	10	0.1
79	4-Br	10	1	1	0.1
80	4-C_2H_5	10	1	10	0.01
81	4-OC_2H_5	10	1		1
82	4-$CH(CH_3)_2$	10	10		10
83	4-Cl		10	10	0.1
84	3,4-$(CH_3)_2$		10		10
85	3,5-$(CH_3)_2$		10		*c*
86	3-CF_3		10		*c*
87	4-C_3H_7		10	10	0.1
88	4-$C(CH_3)_3$		*c*		*c*

[a] See Procedures section for description of rating system. [b] Data averaged from two-four tests. [c] Rating <1.0 at 10-μg level.

juvenilization in *O. fasciatus* (equivalent to a rating of 3.0 for *Oncopeltus* and 4.0 for *Tenebrio*). When the same dosage of a number of chemicals caused maximum juvenilization, the ranking was decided by the dosage that caused the highest intermediate rating (<3 but ≥1). Also listed is the dosage required to cause at least a 1.0 rating, i.e., the lowest rating that showed morphological changes associated with JH activity for either insect.

Earlier work described juvenilizing effects of aryl terpenoid ethers where the side chain was geranyl, citronellyl, or ethylgeranyl (Redfern et al., 1971; Menn and Beroza, 1972; Sarmiento et al., 1973), i.e. where the chain length was 12 or 13 atoms (excluding aryl substituents) and the terpenoid methyl branch that occurs every four carbon atoms could be rationalized as continuing into the benzene ring (Sláma et al., 1974). The chemicals in this study depart from that system by extending the distance between the internal methyl branch and the benzene ring by two carbon atoms. The molecules still retain terpenoid characteristics in the side chain and can be looked on most conveniently as vinylogues of citronellyl aryl ethers.

Certain meta-substituted aryl terpenoid ethers were very effective against *O. fasciatus* and were more active than the corresponding para-substituted ethers (Menn and Beroza, 1972). Other isolated examples of meta-substituted aryl terpenoids showing more JH activity than their para counterparts can be found in Bull et al. (1973) and in Patterson and Schwarz (1977) in tests against *Lygus lineolaris*, *Geocoris punctipes*, and *Rhodnius prolixus*. All of these are hemipteran insects, which may be significant. The data for *O. fasciatus* tests in Table I represent the first examples, to the authors' knowledge, that show the predominant influence on JH activity of meta-substituted aryl terpenoid ethers compared with that of the corresponding para-substituted isomers. In each series comparison of activity due to substituent position can be made with six isomers. The higher activity of the meta-substituted ethers was least pronounced, although still marked, in series I and the activity of **2** vs. **5** was the only example of a para-substituted ether showing higher activity than its meta-substituted isomer. In series II, **27** and **28** were equally active but in the other comparisons in series II, III, and IV the meta-substituted ethers were 10–1000 times more effective in producing maximum juvenilization than their para-substituted isomers.

Because of the relative ineffectiveness of these chemicals against *Tenebrio* most of the structure–activity discussion will be concerned with the data for *Oncopeltus*.

The effect on activity of derivatizing the 8,9-olefinic bond of the parent compounds of series I will be considered first. As in other studies, the epoxy derivatives were generally more active than the olefinic precursor. Compounds **23–28** and **30** were 100 times more active than the corresponding olefins. Maximum activity was found with compounds **23** and **24** (ratings of 2.0 and 1.8 at 0.0001 μg/insect). The effect of the epoxy group was striking; compounds **23–28** cause maximum juvenilization at the nanogram level. The extent of the exceptional activity of this series of chemicals was demonstrated in that 18 of 22 epoxy ethers caused maximum juvenilization at dosages of 0.1 μg or less. Chemicals **29**, **34**, **39**, **41**, and **42** were a curiosity in that there was no increase in activity over that of their olefinic precursors. Adding the elements of methanol or ethanol to the 8,9-position of the side chain had a variety of effects but generally resulted in a JH mimic less active than the parent olefin. The seven exceptions where equal or increased activity was obtained are noteworthy in that five are meta-substituted. The *m*-OCH_3 derivatives **45** and **67** were the most active of series III and IV, causing maximum juvenilization at a 0.01-μg dosage. Surprisingly, the *p*-OCH_3 deriviatives **13**, **41**, **52**, and **73** had identical ratings in all four series.

Chain length has been suggested as a critical feature of a molecule in achieving high JH activity and it has been suggested that the optimum chain length will vary for different insect species, e.g., a chain length of 15 atoms is

optimum for *Tenebrio* and one of 13 atoms for *Oncopeltus* (Wakabayashi et al., 1971; Schwarz et al., 1971). Sláma et al. (1974) suggest that the overall molecular shape, with key structural features located at critical positions or distances along the chain, quite possibly plays the dominant role in causing highest JH activity. Compounds **23–30** have chain lengths of 15 to 17 atoms, which supports Sláma's suggestion that there should be less importance associated with the ultimate chain length needed for optimum activity, especially for the aryl-terpenoid type of compound. In this instance chain length is referred to as the number of carbon or heteroatoms in the backbone of the molecule extending through the benzene moiety and including the phenyl substituents. The extremely high effectiveness of 8-alkoxygeranyl aryl ethers (chain length 16 and 17) against *Tenebrio* (Sarmiento et al., 1973) also supports this contention. It is most likely a happy blending of several variables that optimize activity for one type of structure against a particular insect species.

While the epoxide group at one end of the chain appears necessary for highest activity, the effect of the aryl substituent at the other end is not so clear. Compounds **23–28** with halogen, alkyl, and alkoxide substituents all provide maximum juvenilization at the same dosage and five are meta-substituted compounds. Interestingly, ethers **27** and **28** are equally effective while the other four meta-substituted ethers **23–26** were 100 to 1000 times more active than the corresponding para isomers. The substituents' contribution to chain length does not appear to be overly important at least within the limits of this study. The unsubstituted ether **37** with a chain length of 14 has substantial activity but 14 compounds in the same series with chain lengths from 15 to 17 atoms are more active; six with chain lengths of 15 to 17 atoms are less active (**37** and **38** are equal in activity). It is apparent, however, that the aryl substituent plays a key role in affecting JH activity. The activity of the unsubstituted compounds **17**, **37**, **53**, and **77** compared to other analogues in each series clearly shows this. In series I and II the majority of substituted analogues are more active and in series III and IV the majority are less active than the phenyl ether. Whether the contribution of the substituent towards maximum interaction at a receptor site is steric (e.g., meta vs. para substitution) or electronic (e.g., acting as nucleophiles or electrophiles for potential binding interactions) or possibly the result of other undefined factors has not been established. The change in lipophilicity a substituent may impart to a molecule must also be considered. In general, the most effective compounds have alkoxy or halogen substituents and both provide a source for potential nucleophilic binding interactions with a substrate via unshared electron pairs in a manner similar to that postulated by Nilles et al. (1976) for the epoxide group. Compound **24**, however, has no unshared electron pairs and its high activity seems to support a steric requirement argument. A combination of substituent interactions (as with the entire molecule) may be responsible for high JH activity.

Because *E* isomers were more active than *Z* isomers in numerous studies, it was proposed that the *E* configuration was necessary for highest activity. This is particularly true in the case of the aliphatic type juvenoids (Sláma et al., 1974). To explore what effect the geometry of the internal double bond has on activity, the corresponding *E* isomers of no. **3**, **8**, **11**, **24**, **25**, and **32** were synthesized. Bioassay data are presented in Table II. Six of the *Z* isomers are substantially more active against *Oncopeltus* and four are substantially more active against *Tenebrio* than are the *E* isomers. The *Z* isomer of no. **32** is 100 times more active against *Tenebrio* than its *E* counterpart. While there are many examples of the *E* isomer being the most active configuration in the aryl terpenoid type juvenoids, most of these deal with trisubstituted olefins. There appears to have been little investigation concerning the effect on JH activity associated with the geometry of the disubstituted olefins of the type presented here. These results are exceptions to the generalization that an *E* configuration is needed for highest activity, which suggests a need to evaluate both isomers until a larger body of information is obtained on this type of aryl alkenyl ether system. It is also possible the isomer activity will reverse, i.e., *E* being > *Z*, against other insect species.

Table II. Juvenile Hormone Activity of Selected *Z,E* Isomers

		dosage (μg) causing juvenilization ratings of[a]			
		O. fasciatus		*T. molitor*	
no.	R	3.0	⩾1	4.0	⩾1
		I[b]			
3	3-OCH_3 (*Z*)	0.01	0.01	10	1
	3-OCH_3 (*E*)	0.1	0.1		10
8	3-C_2H_5 (*Z*)	0.1	0.1	1	1
	3-C_2H_5 (*E*)	0.1	0.1		10
11	4-C_2H_5 (*Z*)	1	0.1	1	0.1
	4-C_2H_5 (*E*)	10	1		10
		II[b]			
24	3-C_2H_5 (*Z*)	0.001	0.0001		10
	3-C_2H_5 (*E*)	0.01	0.001		10
25	3-OCH_3 (*Z*)	0.001	0.0001		1
	3-OCH_3 (*E*)	0.01	0.001		1
32	4-C_2H_5 (*Z*)	0.1	0.01	0.1	0.01
	4-C_2H_5 (*E*)	0.1	0.1	10	1

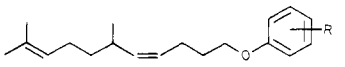
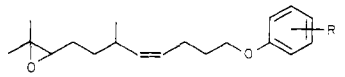
[a] See Procedures section for description of rating system. [b] See Table I for structures.

One factor that may account for the decreased activity of the *E* isomer is its increased chain length compared to that of the *Z* isomer. A similar, but much more pronounced, decrease in activity was observed when the side chain of the *Z* isomer was extended by one methylene unit for a selected group of compounds. The chain extension effectively increases the distance between the internal double bond and the phenoxy group. The bioassay data are given in Table III. Activity is markedly decreased but the activity pattern still follows that shown in Table I. The meta-substituted compounds are much more active against *Oncopeltus* than those with para substituents. With the exception of the methylenedioxy derivatives (no. **89** and **98**), the epoxides are more active than their olefinic precursors. Compound **29** also showed no increase in activity over no. **1** (Table I).

The effect of replacing the ether linkage was investigated briefly. The hydrocarbon analogues of no. **17** and **37** were synthesized and found to be about equal to the ethers in activity against *Oncopeltus* but slightly less active against *Tenebrio*.

As has been well established, potent activity by a JH mimic against one species of insect does not mean it will be active against another, even within the same family. The *Tenebrio* data in Table I, although for an insect of a different order, are a good example. The chemicals were generally effective only at relatively high dosages. Compound **32** was the most active JH mimic against *Tenebrio* in these trials, which supports results of earlier studies where *p*-ethyl derivatives were very active against *Tenebrio*. Only seven other chemicals caused maximum juvenilization at the 1-μg dosage. The 9-ethoxy analogues

Table III. Juvenile Hormone Activity of 6,10-Dimethyl-4,9-undecadienyl and 6,10-Dimethyl-9,10-epoxy-4-undecenyl Aryl Ethers

		dosage (μg) causing juvenilization ratings of[a]			
		O. fasciatus		*T. molitor*	
no.	R	3.0	≥1	4.0	≥1
					
89	3,4-OCH_2O	0.1	0.1		1
90	3-C_2H_5	1	0.1		10
91	3-OCH_3	10	1		10
92	3-CH_3	10	10		10
93	3-Cl		10		10
94	4-CH_3		10		10
95	4-C_2H_5		*b*	10	1
96	4-Cl		*b*		10
					
97	3-C_2H_5	0.1	0.01		1
98	3,4-OCH_2O	0.1	0.1		1
99	3-OCH_3	1	1		10
100	3-CH_3	10	1		10
101	3-Cl	10	1		10
102	4-CH_3	10	10		1
103	4-C_2H_5		1	10	1
104	4-Cl		1		10

[a] See Procedure section for description of rating system. [b] Rating <1.0 at 10-μg level.

(series IV) are the most active group in Table I against *Tenebrio* and show the enhanced activity of the para-substituted ethers relative to the meta-substituted ethers.

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Insecticide Toxicity and Degradation in Houseflies as Affected by Naturally Occurring Food Plant Components

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Studies were conducted to investigate the effects of the naturally occurring food plant components myristicin and *d*-carvone on the toxicity and in vivo degradation of parathion and paraoxon in houseflies. Simultaneous topical application of myristicin and paraoxon, or feeding diets containing myristicin followed by paraoxon application, caused substantial increases in the toxicity of paraoxon. LD_{50} values indicated a tenfold increase in paraoxon toxicity due to a topical application of myristicin at a sublethal dosage of 2 μg/fly. Degradation of [^{14}C]paraoxon was inhibited in flies fed myristicin, resulting in its increased toxicity. With parathion, simultaneous application of myristicin increased housefly mortalities, while feeding this natural compound to flies followed by application of the insecticide resulted in decreased mortalities. Feeding myristicin inhibited the metabolism of [^{14}C]parathion and presumably the production of its toxic analogue, paraoxon. Contrary to results obtained with myristicin, feeding *d*-carvone increased the toxicity and metabolism of parathion, but had no apparent effect on paraoxon toxicity or its degradation. Data reported indicate that some compounds occurring naturally in food plants have the ability to alter the toxicity of insecticides as a result of their effects on insecticide degrading systems.

The presence of naturally occurring, insecticidal plant components has been recognized for centuries (Jacobson and Crosby, 1971). Some of these compounds such as nicotine, rotenone, and the pyrethrums have been commercialized for insect control. In more recent years, compounds having insecticidal activity were isolated in this laboratory from edible portions of some food plants, belonging to the Cruciferae and Umbelliferae plant families.

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