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Azadiene Chemistry. 4. Insecticidal Activities and Chemical Reactivities of Azaaldrin and Azadieldrin. Comparison with Aldrin and Dieldrin

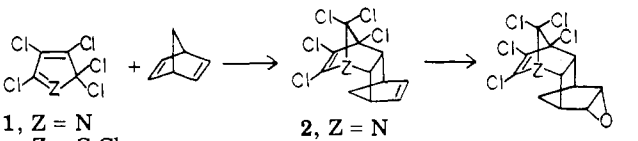
Charles M. Gladstone and John L. Wong*

This paper relates to azaaldrin (**2**) and azadieldrin (**3**) which are bridgehead nitrogen analogues of the once-popular insecticides aldrin (**2a**) and dieldrin (**3a**) whose use has been stringently regulated because of the residue problem. In Scheme I is shown the conversion of 2,3,4,5,5-pentachloro-1-azacyclopentadiene (**1**) to **2** and **3**. The hydrogen-bonding capacity of **2** and **3** was demonstrated by a gas chromatographic technique on a Carbowax 20M column relative to an SE-30 column. This and the enhanced hydrophilicity of the aza compounds, as measured by their solubility properties, are the results of the nitrogen lone pair in **2** and **3**. Another favorable impact of the bridgehead nitrogen can be seen in the hydrolytic behavior of these chlorinated insecticides in an alkaline medium (homogeneous or heterogeneous) in the presence of visible light at 26 °C, e.g. the hydrolysis of **3** proceeds 2.3 times faster than **3a**, and **2** is 1.7 times faster than **2a**. Both aza compounds, when tested on ten common insect pests and rated against standards such as diazinon, methoxychlor, and methylparathion, have shown some very useful activities. However, the aza compounds are not superior to the carbocyclic analogues in several tests, indicating that the lack of a chlorine atom at the bridgehead may have caused some loss of spatial fit into the neuron sites. Also interesting is the fact that azadieldrin (**3**) is ~12 times less toxic than dieldrin (**3a**) on dermal application to rats, thus reducing hazard to users and wildlife.

Aldrin and dieldrin are well-known insecticides conventionally used for the control of soil insects and a variety of household, vegetable, and field crop pests. However, these hydrocarbon insecticides have been found to be disadvantageous due to the accumulation of their residues in the environment, thus posing a threat to the general health. As a consequence, the use of these compounds has been stringently regulated.

Both aldrin and dieldrin belong to the family of chlorinated hydrocarbon insecticides considered to be neurotoxins. They may enter the system of the insect either by mouth or by penetration of the cuticle or lipophilic outer covering of the insect to bind to the axonic membrane of the nervous system (Telford and Matsumura, 1970). It is therefore desirable to have the insecticide lipophilic enough to penetrate the cuticle but also hydrophilic enough to be transported to the locus of activity. However, the structure–activity relationship of these insecticides appears to be very complicated; no definitive rule other than structural similarity of active compounds is available (Matsumura, 1975). This paper relates to azaaldrin and azadieldrin which are bridgehead nitrogen analogues of aldrin and dieldrin. The similar molecular topography of these compounds allows reasonable prediction of insecticidal activity for the new aza compounds. Several favorable effects are plausible: (1) the nitrogen lone pair may enhance hydrophilicity as well as complexation equilibrium constant to the ganglia receptor sites via hydrogen bonding, (2) the nitrogen, in conjunction with the vicinal dichloromethano bridge, constitutes a new functional group for hydrolysis in the otherwise resistant carbocyclic system $-NCCl_2- \rightarrow -NH + -CO_2H$, and (3) the nitrogen itself as well as the adjacent dichlorovinyl π bond being polarized by the inductively withdrawing nitrogen may provide new sites for microbial degradation. Unlike an enamine, the nitrogen is restricted by the bridgehead configuration. We report herein the chemical reactivities and insecticidal activities of azaaldrin and azadieldrin. Comparisons with the carbocyclic analogues will also be presented.

Scheme I



1, Z = N
1a, Z = C-Cl
2, Z = N
2a, Z = C-Cl
3, Z = N
3a, Z = C-Cl

RESULTS AND DISCUSSION

Conversion of 2,3,4,5,5-Pentachloro-1-azacyclopentadiene (1) to Azaaldrin (2) and Azadieldrin (3). As shown in Scheme I, the conversion of **1** → **2** → **3** is well grounded in the format of the Diels–Alder reaction of hexachlorocyclopentadiene (**1a**) with norbornadiene to

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Table I. Comparison of Gas Chromatographic and Solubility Properties of Azaaldrin and Azadieldrin with Their Carbocyclic Analogues

Chlorinated insecticides	GC retention time, min: SE-30 column[a]	GC retention time, min: Carbowax 20M column[b]	Solubility[c]: Petroleum ether, % (w/v)	Solubility[c]: Water, ppm
Azaaldrin (2)	17.5	11.9		
Aldrin (2a)	21.0	10.2		
Azadieldrin (3)	19.3	15.5	0.7 ± 0.1	2.0 ± 0.2
Dieldrin (3a)	22.4	13.4	3.0 ± 0.2	0.3 ± 0.1

[a] T_C = 175 °C, T_D = 270 °C, T_I = 240 °C, and nitrogen flow at 30 ml/min. [b] T_C = 195 °C, T_D = 195 °C, T_I = 220 °C, and nitrogen flow at 40 ml/min. [c] Determined at 22-24 °C. 2 and 2a were not studied since the behavior of azaaldrin was found to be very similar to that of azadieldrin.

yield aldrin (**2a**), which is subsequently oxidized to form dieldrin (**3a**) (Lidov, 1954). The starting azadiene **1**, known earlier as "pentachloropyrrole", was made either by reacting succinimide or dichlorosuccinimide with phosphorus pentachloride (Anschutz and Schroeter, 1896) or by chlorination of pyrrole (Mazzara, 1906). No physical data other than a boiling point are known in the literature. It has now been characterized as follows: bp 92 °C (11 Torr); λ_{max} 282 (ϵ 1000) and 220 nm (ϵ 3000); ν 1610 (C=N), 1520 (C=C), and 1240 cm^{-1} (C—N); $M^{\cdot+}$ 237; and ^{13}C NMR (δ Me_4Si = 0) C-2 164.04, C-3 125.29, C-4 151.06, and C-5 98.33. This ^{13}C spectrum is particularly diagnostic of structure **1**. Also revealing is the difference in the two double bond stretching fequencies shown above, i.e. $\Delta\delta$ 90 cm^{-1}, which falls in with the cyclic 1-azadiene group ($\Delta\delta$ 90–125 cm^{-1}) but not with the 2-azadiene ($\Delta\delta$ 25–70 cm^{-1}) as generalized earlier (Wong and Ritchie, 1970; Wong et al., 1971). Its reaction with water to yield dichloromaleimide quantitatively also confirms the assignment of **1**. Heating **1** in norbornadiene (1 equiv or excess) at 80–90 °C overnight gave a quantitative cycloaddition reaction. The adduct **2**, after recrystallizations from aqueous ethanol, was obtained pure in ~70% yield. Treatment of **2** with *m*-chloroperbenzoic acid in chloroform for 4 days at 25 °C led to complete conversion of **2** to the epoxy derivative **3**. The nitrogen was not affected. Comparison of the IR, ^1H and ^{13}C NMR, and mass spectra of the aza derivatives with those of aldrin (**2a**) and dieldrin (**3a**) allows the assignments of **2** and **3** for azaaldrin and azadieldrin, respectively, as shown in Scheme I.

Hydrogen Bonding, Hydrophilicity, and Hydrolyzability of Azaaldrin (2) and Azadieldrin (3). In Table I are shown the gas chromatographic and solubility properties of the title compounds as well as those of aldrin and dieldrin. On a SE-30 column (silicone gum rubber) which separates principally by molecular weight differences, the aza derivatives showed shorter retention times than their carbocyclic analogues under the same conditions. This is predictable on the basis that the nitrogen compounds are short one chlorine atom. However, on a Carbowax column where the stationary phase hydroxyl groups can hydrogen bond to the nitrogen lone pair to form complexes, longer retention on the column is expected for the aza derivatives. This was observed. As the nitrogen replaces the bridgehead C–Cl group, the solubility properties also undergo some significant changes. Thus, azadieldrin (**3**) is ~7 times more soluble in water than dieldrin (**3a**), but the latter is ~4 times more soluble in petroleum ether, a nonpolar lipophilic medium. Such

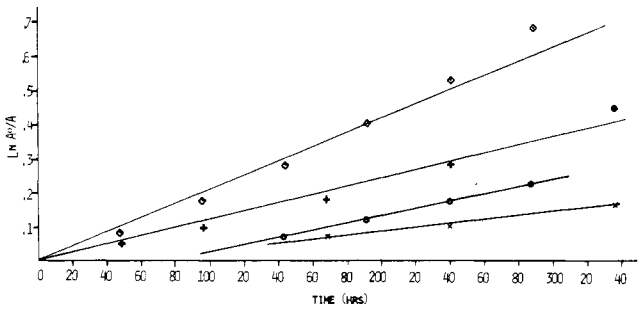

Figure 1. Hydrolysis plot of ln $A°/A$ vs. time for azaaldrin (**2**) (+), aldrin (**2a**) (×), azadieldrin (**3**) (◇), and dieldrin (**3a**) (○) in 0.1 N NaOH (dioxane–water (60:40), induced by a 300-W GE reflector flood lamp. Concentration of substrates ≃ 5 × 10^{-2} M. Reaction progress was followed by GLPC peak area.

Table II. Comparison of Hydrolysis Rate of Azaaldrin and Azadieldrin with Their Carbocyclic Analogues

Chlorinated insecticides	Homogeneous system[a]: $k \times 10^{-7}$, s^{-1}	Homogeneous system[a]: $t_{1/2}$, days	Heterogeneous system[b]: $k \times 10^{-7}$, s^{-1}	Heterogeneous system[b]: $t_{1/2}$, days
Azaaldrin (2)	3.46	23.2	3.31	24.2
Aldrin (2a)	2.08	38.6	1.45	55.3
Azadieldrin (3)	6.85	11.7		
Dieldrin (3a)	3.02	26.6		

[a] Hydrolysis carried out in 0.1 N NaOH (60:40 dioxane-water) at 26 °C on substrates at ~5 × 10^{-2} M, irradiated by a 300-W GE reflector flood lamp. [b] Hydrolysis carried out at 26 °C on substrates at ~5 × 10^{-2} M in 60:40 dioxane-water containing 25 mg/ml of lime (CaO) in suspension, irradiated with a 300-W GE reflector flood lamp.

enhanced hydrophilicity and hydrogen-bonding capacity of **2** and **3** relative to **2a** and **3a** must be attributed to the nitrogen lone pair. In field applications of the insecticides, these properties may be manifested in terms of better bonding to the soil, better transport and complexation to the receptor site, etc.

Another favorable impact of the bridgehead nitrogen can be seen in the pseudo-first-order kinetic plot (Figure 1) for the hydrolysis of these chlorinated insecticides: the aza compounds **2** and **3** as well as the carbocyclic analogues **2a** and **3a**. The hydrolyses were conducted under visible light in an alkaline medium at 26 °C and the disappearance of the substrates was followed by gas chromatography after extracting the aqueous solution with chloroform. No new peaks other than the substrate's appeared on the chromatogram. The changes in substrate concentrations were linear over a prolonged period, with the aza compounds running ahead of their corresponding carbocyclic analogues. Table II shows the rate constants and $t_{1/2}$'s for the above reactions. It can be seen that hydrolysis of **3** proceeds 2.3 times faster than **3a**, and that **2** is 1.7 times faster than **2a**. Also shown in Table II are the hydrolyses of **2** and **2a** in a heterogeneous system, where a lime suspension was used as base. It is interesting to note that k(**2**) values in both the homogeneous and heterogeneous systems are almost the same, yet k(**2a**) increases by 43% in going from the heterogeneous lime to the alkaline solution. Since this hydrolysis is base induced and base is consumed due to HCl liberated, the difference in hydrolytic behavior between **2** and **2a** may be accounted for by the lime surface being able to bind **2** efficiently via hydrogen bonding to the bridgehead nitrogen but not **2a**. It should be noted that aldrin and dieldrin are not known to undergo hydrolytic degradation of the carbon skeleton.

Table III. Action of Azaaldrin, Azadieldrin, and Their Carbocyclic Analogues on the Housefly (*Musca domestica*)[a]

Concn, %	% effects							
	Aldrin (2a)		Azaaldrin (2)[b]		Dieldrin (3)		Azadieldrin (3a)[b]	
	KD[c]	Kill[d]	KD	Kill	KD	Kill	KD	Kill
0.1%			100	100			100	100
0.05			98	94			90	90
0.01			50	68			20	90
0.005	30	94			94	94	0	90
0.001	2	88			2	86	0	20
0.0005	0	62			0	80		
0.0001	0	0			0	24		

[a] See Experimental Section for testing conditions. [b] LC_{50}: azaaldrin, 0.0052; azaldieldrin, 0.002. [c] Knockdown observation. [d] The 24-h mortality may be from residual as well as direct contact.

Table IV. Action of Azaaldrin, Azadieldrin, and Diazinon on Housefly Larvae

	LD_{90}, ppm[a]	Mortality, % control killed[b]
Azaaldrin (2)	16	77
Azadieldrin (3)	40	80
Diazinon	10	37

[a] See Experimental Section for testing conditions. [b] Seven-day exposure to soil treated with insecticide at 40 ppm.

Table V. Action of Azaaldrin, Azadieldrin, and Their Carbocyclic Analogues on the Argentine Ant (*Iridomyrmex humilis*)[a]

	Mortality count, %		
	15-min exposure	1-h exposure	3-h exposure
Aldrin (2a)	0	93	100
Azaaldrin (2)	0	77	100
Dieldrin (3a)	0	100	100
Azadieldrin (3)	0	93	100

[a] See Experimental Section for testing conditions.

Table VI. Action of Azaaldrin and Azadieldrin on the German Cockroach (*Blatella germanica*)[a]

Concn, %	Azaaldrin (2), % killed	Azadieldrin (3), % killed
0.1	80	100
0.05		100
0.01		80

[a] See Experimental Section for testing conditions.

However, Nagl et al. (1970) showed that dieldrin underwent photodechlorination and photocyclization involving the methylene bridge carbon and the dichlorovinyl moiety when irradiated at <300 nm. No such photodieldrins were formed at longer wavelengths (300–400 nm), although dissociation of C–Cl bonds into radicals was proposed. The present requirement of light and base for the above hydrolytic degradations indicates that dechlorination to yield a carbon radical may initiate the final breakdown of the polycyclic system to a carboxylic acid which stays in the alkaline aqueous layer. In the absence of base, the HCl formed might generate enough chlorine atoms under continuing irradiation to reverse the dechlorination, hence establishing an equilibrium condition under which no further degradation is possible. The identity of the degradation products and the mechanism leading to their

Table VII. Action of Azaaldrin, Azadieldrin, and Their Carbocyclic Analogues on the Last Stage Larvae of *Diabrotica u. undecimpunctata*[a]

	Concn, ppm	Mortality, % control killed[b]
Aldrin (2a)	6	70
	2	70
Azaaldrin (2)	6	20
	2	0
Dieldrin (3a)	6	20
	2	30
Azadieldrin (3)	6	20
	2	0

[a] See Experimental Section for testing conditions.

Table VIII. Action of Azaaldrin, Azadieldrin, Methoxychlor, and Methylparathion on Potato Beetle Larvae (*Leptinotarsa defecta*)[a]

	Concn, ppm	Mortality, % control killed[b]	LD_{90}, ppm
Azaaldrin (2)	32	100	9.0
	12.8	93	
	5.1	60	
	2	6	
Azadieldrin (3)	32	100	4.7
	12.8	100	
	5.1	93	
	2	40	
Methoxychlor	32	100	17
	12.8	60	
	5.1	0	
	2	0	
Methylparathion	32	93	30
	12.8	33	

[a] See Experimental Section for testing conditions.

Table IX. Action of Azaaldrin, Azadieldrin, and Their Carbocyclic Analogues on the Southern Army Worm (*Prodenia eridania*)[a]

Concn, %	% control killed			
	Aldrin (2a)	Azaaldrin (2)[b]	Dieldrin (3a)	Azadieldrin (3)[b]
0.1		100		100
0.05	100	100	100	100
0.01	100	20	100	100
0.005	80		100	90
0.001	70		70	
0.0005	0		0	
0.0001				

[a] See Experimental Section for testing conditions. [b] LC_{50} (%): azaaldrin, 0.014; azadieldrin, 0.001–0.005.

Table X. Action of Azaaldrin, Azadieldrin, and Methylparathion on Alfalfa Weevil Adults at 2000 ppm[a]

	% control killed		
	1 day	3 days	7 days
Azaaldrin (2)	26	26	0
Azadieldrin (3)	86	46	6
Methylparathion	60	13	0

[a] See Experimental Section for testing conditions.

Table XI. Action of Azadieldrin on the Boll Weevil[a]

Concn, %	% control killed
0.1	100
0.01	100
0.005	93

[a] See Experimental Section for testing conditions.

Table XII. Action of Azaaldrin on the Body Louse (*Pediculus humanus humanus L.*)[a,b]

Knockdown time	Days effective
1 h	>31 days

[a] See Experimental Section for testing conditions. [b] Standards (malathion and DDT) are also effective for >31 days.

formation will be the subject of future study.

Insecticidal Activities and Animal Toxicity. Azaaldrin (2) and azadieldrin (3) were examined for their activities against housefly (Table III), housefly larvae (Table IV), Argentine ant (Table V), German cockroach (Table VI), cucumber beetle larvae (Table VII), potato beetle larvae (Table VIII), southern army worm (Table IX), alfalfa weevil (Table X), boll weevil (Table XI, for 3 only), and body louse (Table XII, for 2 only). Some very useful insecticidal activities have been demonstrated. Azadieldrin (3) is the more active of the two aza derivatives, and, in the cases where diazinon, methoxychlor, or methylparathion were used as standards, 3 was found to be more potent. Comparisons with aldrin and dieldrin were made in four tests (Tables III, V, VII, and IX), but the activities of the aza compounds are not superior. Despite the many attributes of the bridgehead nitrogen as shown above, the lack of a chlorine atom at the bridgehead may have caused some loss of spatial fit into the receptor site in the nervous system. On the other hand, animal toxicity comparison between 3 and **3a** is more favorable. Klimmer (1971) showed that dieldrin (**3a**) is well absorbed by the gastrointestinal tract and that its oral LD_{50} in male rats is 40–90 mg/kg, depending on the solvent used and on fasting time. With an LD_{50} of 67 mg/kg for fasting rats and dimethyl sulfoxide as solvent, the acute oral toxicity of azadieldrin (3) is close to that of dieldrin (**3a**). However, without showing any symptoms, male rats tolerated a single dermal application of 714 mg/kg of 3, which was the maximum applicable dosage with dimethyl sulfoxide. The dermal toxicity of **3a** in dissolved form at 60 mg/kg is surprisingly high (Klimmer, 1971). Therefore, the problems of endangering the users and wildlife will be much less with azadieldrin. Considering the various advantageous chemical reactivities and biological activities demonstrated by azaaldrin and azadieldrin, it appears that the present substitution of a nitrogen for a bridgehead C–Cl group in aldrin and dieldrin is a modification in the right direction.

EXPERIMENTAL PROCEDURE

^1H NMR spectra were obtained using a Varian A-60A spectrometer or a Perkin Elmer R-12 spectrometer. ^{13}C NMR spectra were determined on a Varian CFT-20 spectrometer, courtesy of Universiy of Kentucky, Lexington, Ky. NMR samples were prepared as 0.5 M solutions in $CDCl_3$ containing 1% tetramethylsilane ($\delta_{Me_4Si} = 0$). IR spectra were run on a Beckman IR-12. Mass spectra were run on a quadrupole mass spectrometer, courtesy of Battelle-Columbus Laboratories, Columbus Ohio. GLPC analyses were performed on a Hewlett Packard 5750 B chromatograph with dual flame ionization detector. All analyses were done on a 6 ft × 0.025 in. aluminum column packed with 20% SE-30 on Chromosorb W AW DMCS or 10% Carbowax 20M on Chromosorb W; other conditions are as noted in the footnotes to Table I. Melting points are uncorrected. Combustion analyses were performed by M-H-W Laboratories, Garden City, Mich.

2β,3β,6β,7β,8α-8,9,10,11,11-Pentachloro-1-azatetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene (Azaaldrin, 2). To 14 g (58 mmol) of 2,3,4,5,5-pentachloro-1-azacyclopentadiene (1) was added bicyclo[2.2.1]hepta-2,5-diene (1 equiv or excess), and the mixture was heated at 80–90 °C for 24 h. The dark brown reaction mixture containing the product was column chromatographed on 150 g of silica gel in hexane. The eluent was evaporated, and the light orange residue was recrystallized from aqueous ethanol to yield 13.0 g (67%) of white, crystalline product: mp 97–99 °C; ^1H NMR ($CDCl_3$–Me_4Si) δ 1.27 (d, 1 H, J = 11 Hz), 2.02 (d, 1 H, J = 11 Hz), 2.68 (d, 1 H, J = 8 Hz), 2.88 (d, 1 H, J = 8 Hz), 2.90 (m, 1 H), 3.12 (m, 1 H), 6.28 (m, 2 H); ^{13}C NMR ($CDCl_3$–Me_4Si) δ 40.81 (d, J = 145 Hz), 41.31 (d, J = 145 Hz), 41.50 (t, J = 140 Hz), 53.30 (d, J = 150 Hz), 54.19 (d, J = 150 Hz), 82.12 (s), 93.65 (s), 105.46 (s), 140.81 (d, J = 175 Hz), 167.65 (s); IR (KBr) 3050, 2990, 2900, 1615, 1575, 1475, 1150, 720 cm^{-1}; mass spectrum m/e 329 (M·$^+$), 228, 101, 91, 66, 65.

Anal. Calcd for $C_{11}H_8NCl_5$: C, 39.81; H, 2.41; N, 4.22. Found: C, 39.99; H, 2.22; N, 4.06.

2β,3β,6β,7β,8α-*exo*-4,5-Epoxy-8,9,10,11,11-pentachloro-1-azatetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodec-9-ene (Azadieldrin, 3). To 6 g (18 mmol) of azaaldrin (2) in 50 ml of chloroform was added 3.90 g (21 mmol, 1.25 equiv) of *m*-chloroperbenzoic acid. The homogeneous solution was allowed to stand for 4 days at 22–24 °C. The solution was extracted with 3 × 50 ml of 5% $NaHSO_3$, 6 × 50 ml of 5% $NaHCO_3$, and 2 × 50 ml of water. The chloroform layer was dried with $MgSO_4$ and evaporated, and the solid residue recrystallized from ethanol–water to yield 5.9 g (94.4%) of white, crystalline 3: mp 158.5–160 °C; ^1H NMR ($CDCl_3$–Me_4Si) δ 1.23 (d, 1 H, J = 12 Hz), 1.48 (d, 1 H, J = 12 Hz), 2.66 (s, 1 H), 2.67 (d, 1 H, J = 7 Hz), 2.87 (s, 1 H), 2.88 (d, 1 H, J = 7 Hz), 3.09, (d, 1 H, J = 3.5 Hz), 3.14 (d, 1 H, J = 3.5 Hz); ^{13}C NMR ($CDCl_3$–Me_4Si) δ 21.00 (t, J = 140 Hz), 36.90 (d, J = 145 Hz), 37.30 (d, J = 145 Hz), 50.49 (d, J = 200 Hz), 50.98 (d, J = 200 Hz), 52.04 (d, J = 150 Hz), 53.31 (d, J = 150 Hz), 81.84 (s), 94.13 (s), 104.56 (s), 167.96 (s); IR (KBr) 2990, 2960, 2900, 1575, 1475, 1150 cm^{-1}; mass spectrum m/e 345 (M·$^+$), 310, 228, 108, 107, 82, 81, 70.

Anal. Calcd for $C_{11}H_8NCl_5O$: C, 37.98; H, 2.30; N, 4.02. Found: C, 38.24; H, 2.21; N, 3.82.

Procedures for Insecticidal Screening. Candidate samples were formulated by dissolving the sample in acetone containing small amounts of emulsifier. The test formulations were then diluted in water to obtain the desired active ingredient concentration. In these tests untreated controls were included for comparative purpose. Specific conditions of testing are described below.

Contact Spray for Housefly, German Cockroach, and Boll Weevil. Diluted samples (500 ppm) were applied to houseflies, cockroaches, and boll weevils in a contact test by means of the Waters vertical spray tower. The spray tower is operated at 10 psi and discharges about 28 ml of material per min through a glass atomizer. The spray descends through an 8-in. stainless steel cylinder to the test insects 44 in. below the atomizer. Fifty adult houseflies were sprayed in a 2 in. high × 5 in. diameter stainless steel cage faced on top and bottom with 14 mesh screen. The insects were retained in the same cages for knockdown observations. The 24-h mortality of houseflies may be from residual as well as from direct contact. The percentages of knockdown and kill are recorded. Similarly, 20 adult cockroaches and 20 adult boll weevils were sprayed in an identical container. The 48-h mortality may be from residual as well as from direct contact.

Soil Mix for Housefly Larvae and *Diabrotica* Larvae. Diluted samples were mixed with soil in 8-oz plastic cups to give the indicated concentrations. With a con-

centration of 40 ppm in the soil, five last stage housefly larvae were placed on top of the soil immediately after sample treatment. The mortality after 48 h was recorded. The treatment was then repeated with five additional larvae and freshly treated soil. Similarly, with soil concentrations of 6 and 2 ppm, the last stage larvae of *Diabrotica u. undecimpuntata* were tested.

Residual Spray on Cardboard for Argentine Ant. One-pint cardboard cartons were sprayed with formulations at the rate of 10 mg/ft^2. Sixteen hours after spraying ants were collected and placed in the treated cartons which were capped with fine nylon netting. Mortality counts were taken after 15 min, 1 h, and 3 h of exposure. Each test consisted of three replicates of 30 ants each.

Leaf Feed for Potato Beetle Larvae and Southern Army Worm. Eggplant leaves dipped into test solutions of the respective compounds were offered to the potato beetle larvae for a 24-h feeding period, after which mortality data were recorded. Each test consisted of three replicates of five larvae each. Lima bean leaves dipped into test solutions of the respective compounds were offered to ten larvae of the Southern army worm (late third instar), for a 48-h feeding period. Mortality data were recorded.

Foliage Spray for Alfalfa Weevil. Potted alfalfa plants were sprayed with the test solutions at 2000 ppm. The plants were then infected with alfalfa weevil adults. Mortality counts were taken at 1, 3, and 7 days post spray.

Contact Test for Body Louse. Compounds were screened as body louse (*Pediculus humanus humanus L.*) toxicants by exposing young adult body lice on treated patches of woolen cloth, 3.8 cm in diameter. Duplicate patches were impaled on pinboards, and 0.7 ml of 1% solutions of the compounds in acetone was applied to them by pipet. After the patches were dried, 10 female lice were exposed to them in 50-ml glass beakers for 24 h. Knockdown was recorded at intervals of 15 min, 1 h, and 3 h, and kill at 24 h. Patches on which all lice were dead or knocked down were retested at intervals of 2 to 7 days until one or more lice remained unaffected. After 31 days the tests were terminated, even if the patches were still effective.

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Formamidine Acaricides. Toxicity and Metabolism Studies with Twospotted Spider Mites, *Tetranychus urticae* Koch

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The toxicity to adult twospotted spider mites of 104 aryl formamidines was studied using a slide-dip technique. For maximum toxicity formamidines must possess an aryl moiety with two substituents, and these two substituents should be located at ring positions two and four. With regard to requirements on the amino nitrogen, it was concluded that at least one substituent should be lower alkyl, preferably methyl, while greater flexibility existed relative to the other amino nitrogen substituent. It could be hydrogen, lower alkyl, methylthiomethyl, or other more complex moieties. Metabolism studies of two aryl formamidines, chlordimeform-^{14}C and *N'*-(4-chloro-*o*-tolyl)-*N*-methylformamidine or demethylchlordimeform-^{14}C, in twospotted spider mites indicated a rapid uptake of each compound accompanied by high internal levels of organosoluble radioactive material. Chlordimeform metabolites included demethylchlordimeform, *N'*-(4-chloro-*o*-tolyl)formamidine, 4'-chloro-*o*-formotoluidide, and 4-chloro-*o*-toluidine. Both chlordimeform and demethylchlordimeform were metabolized slowly by twospotted spider mites as compared with houseflies, a chlordimeform-tolerant insect. Differential metabolism likely plays a role in the selective toxicity of chlordimeform.

There are numerous problems associated with acarine (mites and ticks) control. For example, phytophagous mites reproduce rapidly and in great numbers. They are regarded as genetically plastic organisms, and new races are continually formed. Therefore, strains resistant to conventional acaricides can develop with such rapidity as to threaten the efficacy of an entire class of chemicals. Thus, there is a continuing search for new classes of acaricides.

The formamidines are a class of compounds active as acaricides and insecticides which differ in their mode of action from the chlorinated hydrocarbons, organophosphates, and carbamates (Dittrich, 1966). Moreover, some formamidines are more toxic to organophosphate-

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