Chapter 21

Fluorinated Sulfonamides

A New Class of Delayed-Action Toxicants for Fire Ant Control

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Fluorinated sulfonamides were discovered to have the delayed toxic activity required to control the fire ant, Solenopsis invicta, a medical and agricultural pest ant species. The large number of fluorinated sulfonamide analogues and derivatives available offer a wide variety of activities (delayed and rapid) and solubilities (water to soybean oil). These compounds were effective against fire ants in laboratory and field tests and one of the compounds is being commercialized. Certain compounds have been demonstrated to be good control agents against other ant species, cockroaches, and mosquitoes.

The fire ants, Solenopsis richteri and S. invicta, were accidentally imported from South America, (probably through the port of Buenos Aires) into the Mobile, Alabama area around 1910 and 1935, respectively. Fire ants normally infest new areas through mating flights during which the queens may fly up to 12 miles (1). However, it was evident from early surveys (2) that spread of the fire ants was accelerated greatly by man through the transportation of nursery stock. Soil on plants harbored new queens or incipiant colonies and these were transported throughout the southern United States. Once isolated populations were established they spread locally through mating flights until all the infestations coalesced. S. richteri proved to be less competitive or adaptable than S. invicta and now occupies only a small enclave in northeastern Mississippi and northwestern Alabama. In spite of federal-state quarantines, recent discoveries of S. invicta infestations in Tennessee, Oklahoma and New Mexico highlight the fact that this fire ant has not yet reached the limit of its northern or western expansion (Homer Collins, APHIS, USDA, personal communication, 1987). A further complicating factor in determining the fire ant's spread was the discovery of hybridization between the two imported fire ants (3). The reproductively viable hybrid has a large, but as yet undefined, range in northern Mississippi, Alabama, and Georgia (Ross, K. G., Vander Meer, R. K., Fletcher, D. J. C., and Vargo, E.

L., Evolution, in press; and *Diffie, S., +Vander Meer, R. K., and *Bass, M. H., *University of Georgia and +USDA). How the hybrid strain will affect the limits of fire ant expansion is under investigation.

Medical Impact. Fire ants have been likened to weeds since they have a high reproductive capacity and their ecology and biology are ideally suited to take advantage of disturbed ecosystems (4). Since man is the greatest disturber of the environment, it follows that man-ant interactions are inevitable. Essentially, everywhere man lives and plays (backyards, playgrounds, parks, golf courses, etc.) or works (gardens and all types of agriculture) become disturbed habitats. The fact that a mound may contain as many as 230,000 workers, and many infested areas commonly have 125 to 150 mounds per hectare insures that there will always be a great deal of contact between fire ants and people in the infested areas (5).

The common name "fire ant" is derived from its painful sting, which causes a burning sensation followed by the formation of a sterile pustule within 24 hours. Approximately 30% of the people in the infested areas are stung by fire ants in a given year (6) and of these 0.61% experience systemic anaphylaxis (7). The venom of fire ants is composed primarily of 2-methyl 6-alkyl or alkenyl piperidine alkaloids (8). These alkaloids cause pustule formation because they are necrotoxic but they also have many other physiological effects (9). Less than 1% of the venom is protein but this small amount can cause severe allergic reactions and occasionally death (5,7,10).

Economic Impact. It is believed that fire ant damage to agricultural crops was masked before the late 1970's because of the prior use of residual insecticides, such as chlordane for control of other insect pests. Since these chemicals are highly toxic to fire ants, they undoubtedly kept these fields free of infestations (6). Current research indicates that fire ants cause economically important losses of soybeans, potatoes, citrus, eggplants, okra, and other vegetable crops. In addition, fire ants have killed newborn calves, pigs, and chickens, attacked the young or eggs of numerous bird species, amphibians and rabbits, damaged highways, and electrical equipment; and can be a pest in homes and hospitals (11).

Control Requirements. Historically, the control of the imported fire ants, S. invicta and S. richteri, in the United States dates back to 1938 when calcium cyanide dust treatments were used to treat individual colonies infesting agricultural land near Mobile, AL (12). A concern with fire ants escalated along with their population until, in 1957, the United States Congress appropriated money for a Federal-State Imported Fire Ant Control Program. The first chemicals used in this program were residual applications of heptachlor or dieldrin (13). These toxicants were replaced in 1963 because of environmental concerns with a bait toxicant system using mirex, which required the use of much less active ingredient (13). Unfortunately, registrations of mirex were cancelled at the end of 1977 because of residues in environmental organisms and possible carcinogenicity (14). This regulatory action resulted in

an intensive search for other toxicants suitable for fire ant baits (15).

The difficulty in finding suitable insecticides for use in baits for fire ants is directly related to the behavior and ecology of the insect. Foraging worker ants represent only a small fraction of a colony's population. Once a foraging ant locates food, other workers are recruited to the food source with the trail pheromone (16). The foraging ants store food in their crops, and through regurgitation and food exchange (trophallaxis), they quickly disperse the material to other members of the colony (5). Because of this system of food gathering which is followed by ingestion, storage and regurgitation, two major qualifications for a toxicant become apparent. If the toxicant acts too quickly, the foraging workers will die before they can distribute the material to other members of the colony and ultimately to the queen. Therefore, delayed toxicity is required. Tests with dyed soybean oil indicated that complete colony distribution is achieved within 24-72 hr. Secondly, the process of trophallaxis greatly dilutes a toxicant (a mature colony may contain more than 230,000 workers) making it necessary to have delayed toxicity over a wide range of dosages (preferably > 100) (17).

TABLE 1. Classification System for Imported Fire Ant Bait Toxicants

Class	Definition
I	Compounds that give insufficient kill at the preliminary concentrations (less than 90% at the end of the test period).
II	Compounds that kill too quickly at the higher concentrations but give insufficient kill at the lower concentrations, that is, higher concentrations give 15% or more kill after 24 hr and 90-100% at the end of the test period, but lower concentrations give less than 90% kill at the end of the test period.
III	Compounds that show no greater than a 9-fold difference between the minimum and maximum concentrations that exhibit delayed toxicity.[a]
IV	Compounds that showed at least a 10-fold but not greater than 99-fold difference between the minimum and maximum concentrations that exhibited delayed toxicity.
V	Compounds that show at least a 100-fold difference between the minimum and maximum concentrations that exhibit delayed toxicity.

[a]Delayed toxicity is defined as mortality of less than 15% after 24 hr and more than 89% at the end of the test period.

As of the end of 1986, our laboratory had screened 6,882 chemicals for the delayed toxicity required for fire ant baits. The following procedures were used: The toxicant was dissolved to the desired concentration in either soybean oil or honey-water (1:1) depending on its solubility. Test groups of 20 worker ants were allowed to feed for 24 hr on cotton swabs saturated with the formulation. After 48 hr, the ants were fed unadulterated soybean oil. Mortality counts were made at 1, 2, 3, 6, 8, 10, 14, 17, and 21 days after the initial exposure. Each material was tested at 3 concentrations: 1, 0.1, and 0.01% (18).

All chemicals tested were classified according to the scheme shown in Table 1. Class I compounds are inactive while Class II materials are good toxicants but do not have the required delayed toxicity. Class III compounds have delayed action, but the concentration range of their activity is too narrow. The type of activity we are looking for in a toxicant is exemplified by a Class IV or V response, i.e., it exhibits delayed toxicity over a wide range of concentrations.

As expected, most (86.6%) of the 8,662 compounds screened fell into the non-toxic Class I category. Less than 0.5% were Classes IV and V.

Fluoroaliphatic Sulfonamide Insecticidal Activity

In the search for delayed-action formulations we experimented with several controlled release techniques (19). One of these projects involved pendant toxicants, in which a fast acting insecticide was chemically bonded to a polymer backbone (20). The polymer-pesticide linkage was in theory supposed to deactivate the toxicant until the organism released the free toxicant via metabolic processes. Few insecticides have functional groups suitable for this purpose; however, our screening program had uncovered several fluorinated primary alcohols active against fire ants (21). One of these compounds was used as a model insecticide to test the pendant-toxicant technique. Poor solubility of the products in soybean oil led to the use of commercially available fluorinated surfactants to aid in the dissolution of the pendant-toxicant. Standard control bioassays uncovered the fact that the fluorinated surfactants themselves had delayed-action toxicity against fire ants. Further investigation led to the discovery of fluorinated sulfonamides, a new class of insecticide with the general structure $R_fSO_2NR_1R_2$.

Several fluorine containing compounds have been shown to have delayed-action toxicity against the fire ant (21,22). One of these, tetrahydro-5,5-dimethyl-2(1H)-pyrimidinone(3-(4-trifluoromethylphenyl)-1-(2-(4-trifluoromethyl) phenyl)ethenyl)-2-propenylidene) hydrazone, has been commercialized (23). In another approach fluoroacetyl derivatives and analogues were designed as pro-insecticides (24). Although there is precedence for delayed-action fluorine containing insecticides, the discovery of the fluorinated sulfones provides a class of compounds with tremendous structural diversity (25).

Synthesis of Fluorinated Sulfonamides. All compounds presented in this paper were prepared and provided by 3M Company. The general class of compound has been known for many years as surfactants (26,27). The general synthetic scheme is as follows:

$$R_fSO_2F + R_1R_2NH \longrightarrow R_fSO_2NR_1R_2$$

The amine can be aliphatic or heterocyclic. If one of the R-groups is a hydrogen, then further derivatization can be made by reaction of the sulfonamide sodium salt with a halide; i.e.

$$R_fSO_2NHR_1 \xrightarrow[2)\ ClCH_2CH_2OH]{1)\ CH_3ONa} R_fSO_2NR_1CH_2CH_2OH$$

The variety of possible reactants provided a large number of compounds for primary screening against fire ants (28).

Primary Delayed-Action Bioassay Results

Over 250 compounds of the general formula, R_fSO_2A, were tested for toxicity against fire ants, where R_f is a fluoroaliphatic radical and A is any compatible chemical structure. The majority of the compounds were fluorinated sulfonamides, $R_fSO_2NR_1R_2$, where R_1 and R_2 can be any compatible structure and $R_f = C_8F_{17}$-. The following is a summary of results for R- groups of like functionality. Unless specified R_f was held constant (C_8F_{17}-).

Alkyl-Substituted Sulfonamides. Class III delayed activity was observed in the methyl-(II), ethyl-(III), isopropyl-(IV), and diethyl-(VI) substituted sulfonamides; however, the t-butyl-analog (V) showed no toxicity (Table 2). The cause of its inactivity is unknown but may be related to increased steric bulk. The active members of this group were close to being in the highly desirable Class IV category.

Unsaturated Hydrocarbon-Substituted Sulfonamides. N-substituents containing double bonds gave either fast or delayed action at 1% concentration (Table 3). Double bonds directly attached to the nitrogen (phenyl (X) and vinyl (VII)) gave fast kill at 1%, whereas the methylene interrupted allyl (VIII), and benzyl (XI) substituents gave excellent delayed activity. The allyl (VIII) analog had Class IV activity.

Aliphatic Alcohol-Substituted Sulfonamides. Several monohydroxy alcohols were tested (Table 4) and gave Class III or IV delayed activity; however, the toxicity was delayed to a greater extent than the corresponding compound without the alcohol group. (Compare XII with III and XIV with II). Because of the combination of N-alkyl and alcohol substituents, it was difficult to draw conclusions about structure-activity relationships. If the R-groups contained two hydroxyls, in any combination, activity was lost (XV).

Polyether-Substituted Sulfonamides. In general the polyether group, either ending in a hydrogen or capped with a methyl group, moderated the activity of the analogous unsubstituted compound in a way similar to the alcohol-substituted sulfonamides (Table 5). In one example, activity was diminished from Class III (III) to

Table 2. Toxicity of Alkyl Substituted Sulfonamides to Fire Ant Workers

Compound	$C_8F_{17}SO_2NR_1R_2$ R1	R2	Conc. %	% Mortality at specified days[a] 1	2	3	6	8	10	14	17	21
I	-H	-H	0.01	0	0	0	3	7	7	10	20	23
			0.1	0	0	0	2	33	77	92	95	98
			1.0	43	85	98	100					
II	-H	$-CH_3$	0.01	0	0	2	3	7	7	7	23	40
			0.1	0	0	7	88	97	98	100		
			1.0	17	93	100						
III	-H	$-C_2H_5$	0.01	0	0	0	0	2	2	10	22	50
			0.1	0	0	2	80	97	97	98	98	100
			1.0	25	100							
IV	-H	$-CH(CH_3)_2$	0.01	2	2	2	2	2	3	5	27	65
			0.1	0	0	10	75	93	98	100		
			1.0	83	97	100						
V	-H	$-C(CH_3)_3$	1.0	0	0	0	0	0	0	0	5	
VI	$-C_2H_5$	$-C_2H_5$	0.01	0	0	0	2	5	10	20	50	60
			0.1	0	7	13	78	92	98	100		
			1.0	30	100							

[a]Percentages are the mean of three replicates. The soybean oil control had <15% mortality at the end of the test, and the mirex standard had normal delayed activity.

Table 3. Toxicity of Unsaturated Sulfonamides to Fire Ant Workers

Compound	$C_8F_{17}SO_2NR_1R_2$ R1	R2	Conc. %	% Mortality at specified days[a] 1	2	3	6	8	10	14	17	21
VII	$-CH_3$	$-CH{=}CH_2$	0.01	0	0	0	8	8	13	25	37	57
			0.1	0	7	33	77	90	92	100		
			1.0	100								
VIII	-H	$-CH_2CH{=}CH_2$	0.01	2	2	2	2	2	2	12	37	75
			0.1	3	3	3	48	60	78	93	98	100
			1.0	13	53	80	100					
IX	-H	$-CH_2C{\equiv}CH$	0.01	5	5	5	5	5	5	15	15	30
			0.1	2	2	2	2	3	5	43	73	87
			1.0	83	87	88	95	97	97	100		
X	-H	$-C_6H_5$	0.01	0	0	0	2	3	3	7	17	27
			0.1	0	2	2	8	53	70	93	95	98
			1.0	83	87	88	95	97	100			
XI	$-C_2H_5$	$-CH_2C_6H_5$	1.0	0	0	0	0	0	3	3	3	3
			0.1	0	0	0	2	2	3	8	18	42
			1.0	0	0	0	2	42	83	100		

[a]Percentages are the mean of three replicates. The soybean oil control had <15% mortality at the end of the test.

Table 4. Toxicity of Mono- and Di-alcohol-substituted Sulfonamides to Fire Ant Workers

Compound	$C_8F_{17}SO_2NR_1R_2$ R1	R2	Conc. %	% Mortality at specified days[a] 1	2	3	6	8	10	14	17	21
XII	$-C_2H_5$	$-C_2H_4OH$	0.01	0	0	2	2	2	2	2	2	3
			0.1	0	0	0	0	2	2	8	40	60
			1.0	0	0	0	45	67	88	98	100	
XIII	$-C_4H_9$	$-C_2H_4OH$	0.01	0	0	0	0	0	0	0	0	2
			0.1	0	2	2	3	3	3	25	48	78
			1.0	0	0	0	0	0	40	93	98	100
XIV	$-CH_3$	$-C_4H_8OH$	0.01	0	0	2	5	8	8	8	10	13
			0.1	0	0	0	2	5	30	75	85	92
			1.0	0	2	10	83	85	95	100		
XV	$-C_2H_4OH$	$-C_2H_4OH$	0.01	0	0	0	2	5	10	35		
XVI	$-CH_3$	$-CH_2CH(OH)CH_2OH$	1.0	0	0	0	2	2	2	5		

[a]See footnote a Table 3.

Class I (XVIII). No trends in activity could be distinguished based on the length of the polyether or whether it contained ethoxy or propoxy units.

Miscellaneous Active Compounds. Many active sulfonamide derivatives did not fall into a convenient functional group category or there were only one or two examples of a category. Results for several of these compounds are shown in Table 6. Compounds XXII to XXVI show a diversity of nitrogen substitutions that in most cases gave excellent delayed activity. Compound XXV gave rapid kill at the 1.0 percent level. We view XXII to XXVI as lead compounds that may be useful in discovering more effective toxicants both in terms of delayed action for fire ant control and fast action for the potential control of other insect pests. Compound XXII is an intriguing example where the nitrogen of the sulfonamide is utilized directly in the imidazole ring. Many other derivatives could be prepared that incorporate the sulfonamide nitrogen into a ring system; i.e. oxazole, piperidine, and pyrrole.

Substituents that Inactivate the Sulfonamides. Only a few of the previously discussed compounds did not have either delayed-action or rapid kill. Table 7 illustrates sulfonamide nitrogen substituents that resulted in inactivity. Substituents containing an amino (XXVII), amide (XXVIII), phosphate (XXIX), or an aromatic carboxylic acid (XXX) group showed no toxicity.

Structural Features Important to Toxicity

Effects of Decreasing the Length of R_f. Of the compounds available, five had an unsubstituted sulfonamide moiety and decreasing fluorocarbon chain lengths. Table 8 illustrates that decreasing the length of R_f decreases the toxicity of the compound compared to $R_f = C_8F_{17}-$. The best activity was obtained when R_f equaled $C_6F_{13}-$ (XXXIV) or $C_8F_{17}-(I)$. Compound XXXI showed some activity, but did not rank higher than Class 1. No corresponding compounds were available that had R_f chains greater than C_8. When the fluoraliphatic portion of the molecule was sandwiched between two methyl sulfonamides, $(CH_3NHSO_2C_4F_8-)_2$, activity was lost, which emphasizes the importance of an unencumbered R_f group.

The Importance of the Fluorocarbon and Sulfone Moiety to Toxicity. The importance of R_f (Table 9) to the toxicity of the fluorinated sulfonamide structure was tested using the hydrogen analogue of compound I. When the fluorines were replaced by hydrogens (XXXV) all activity was lost. The activity found in compound XXXI was diminished by the removal of one of the three fluorines (XXXVI). Similarly when the sulfone moiety was replaced with a carbonyl group (XXXVII), activity was lost. Interestingly, bioassays of the corresponding sulfonic acid (XXXVIII) or its potassium salt (XXXIX) in honey water (required because of a lack of solubility in soybean oil) gave very good delayed activity. Although these water soluble compounds are not suitable for fire ant control, they offer potential for the control of other insect pests, especially those associated with water. These results point out

Table 5. Toxicity of polyether-substituted sulfonamides to Fire Ant Workers

Compound	$C_8F_{17}SO_2NR_1R_2$ R1	R2	Conc. %	% Mortality at specified days[a] 1	2	3	6	8	10	14	17	21
XVII	$-C_2H_5$	$-(C_2H_4O)_3H$	0.01	0	0	0	0	3	7	7	13	20
			0.1	0	0	0	0	0	0	3	7	27
			1.0	0	0	2	52	87	98	99	100	
XVIII	$-C_2H_5$	$-C_2H_4O(C_3H_6O)_8H$	0.01	0	0	0	0	0	0	0	0	0
			0.1	0	0	0	0	0	0	0	3	17
			1.0	0	0	0	3	5	23	37	45	60
XIX	$-C_4H_9$	$-C_2H_4O(C_3H_6O)_8$	0.01	0	0	2	2	2	2	2	2	2
			0.1	0	0	0	0	0	3	3	15	45
			1.0	0	2	2	2	2	40	87	97	100
XX	$-C_2H_5$	$-(C_2H_4O)_7CH_3$	0.01	2	3	3	3	3	5	8		
			0.1	3	5	8	15	20	23	40		
			1.0	2	5	5	38	57	80	88		
XXI	C_2H_5	$-(C_2H_4O)_{17}CH_3$	0.01	0	0	0	3	7	7	10	13	17
			0.1	0	0	0	2	3	5	10	25	48
			1.0	0	0	32	100					

[a]See footnote a Table 2.

Table 6. Toxicity of Some Miscellaneous Active Sulfonamides to Fire Ant Workers

Compound	$C_8F_{17}SO_2NR_1R_2$ R1	R2	Conc. %	% Mortality at specified days[a] 1	2	3	6	8	10	14	17	21
XXII		-CH=CHN=CH- (imidazole)	0.01	2	3	3	8	8	8	13	15	18
			0.1	0	2	3	10	10	52	67	80	88
			1.0	0	2	17	92	100				
XXIII	-H	$-CH_2N$ (O, CH_2CH_2, CH_2CH_2)	0.01	0	0	0	0	0	0	0	0	
			0.1	0	0	0	0	0	10	30	73	
			1.0	7	35	50	50	92	97	100		
XXIV	-H	$-C(=O)NHC_6H_{11}$ (oyolic)	0.01	0	0	0	2	2	7	10		
			0.1	0	0	0	28	40	60	85		
			1.0	2	5	18	62	70	93	100		
XXV	-H	$-C_2H_4Cl$	0.01	0	0	0	0	3	3	5	23	47
			0.1	0	0	2	22	83	95	97	100	
			1.0	57	87	98	100					
XXVI	-H	$-SCCl_3$	0.01	0	0	2	2	2	2	7		
			0.1	0	2	5	43	65	70	80		
			1.0	7	25	97	100					

[a]See footnote a Table 2.

Table 7. Toxicity of Inactive Substituted Sulfonamides to Fire Ant Workers

Compound	$C_8H_{17}SO_2NR_1R_2$ R1	R2	Conc. %	% Mortality (days) 1	2	3	6	8	10	14
XXVII	-H	$C_2H_4NH_2$	1.0	2	2	2	2	2	2	10
XXVIII	$-CH_3$	$C_2H_4C(=O)NH_2$	1.0	0	0	0	0	3	5	10
XXIX	$-C_2H_5$	$C_2H_4OPO_3H$	1.0	2	3	3	3	3	3	10
XXX	$-C_2H_5$	$CH_2-C_6H_4-CO_2H$	1.0	0	0	0	0	2	2	2

[a]See footnote a Table 2.

Table 8. Effects of Decreasing the Fluorocarbon Chain Length on Toxicity to Fire Ant Workers

Compound	Structure	Conc. %	% Mortality at specified days[a] 1	2	3	6	8	10	14	17	21
XXXI	$CF_3SO_2NH_2$	0.01	0	0	0	3	3	5	7	8	17
		0.1	3	3	3	5	5	5	17	27	58
		1.0	2	8	18	33	42	50	67	73	82
XXXII	$C_2F_5SO_2NH_2$	1.0	3	17	22	35	40	45	50		
XXXIII	$C_4F_9SO_2NH_2$	0.01	0	0	0	3	3	3	5		
XXXIV	$C_6F_{13}SO_2NH_2$	0.01	0	0	0	2	2	2	2	5	12
		0.1	3	7	7	7	7	17	63	77	92
		1.0	0	3	30	67	75	87	95	98	100
I	$C_8F_{17}SO_2NH_2$	0.01	0	0	0	3	7	7	10	20	23
		0.1	0	0	0	2	33	77	92	95	98
		1.0	43	85	98	100					

[a]See footnote a Table 2.

Table 9. Importance of Fluorocarbon and Sulfone Moiety of Molecules on Toxicity

Compound	Structure	Conc. %	% Mortality at specified days[a] 1	2	3	6	8	10	14	17	21
XXXV	$C_8H_{17}SO_2NH_2$	1.0	5	7	8	12	12	12	12		
XXXVI	$HCF_2SO_2NH_2$	1.0	0	2	2	13	18	20	30		
XXXVII	$C_7F_{15}C(=O)NH_2$	1.0	0	0	0	2	2	2	2		
XXXVIII	$C_8F_{17}SO_3H^b$	1.0	0	37	62	95	100				
XXXIX	$C_8F_{17}SO_3H^b$	1.0	2	2	23	87	100				

[a]See footnote a Table 2
[b]Formulated in honey water.

that the insecticidal activity of this class of compounds resides in the basic R_fSO_2A formula, and that the sulfonamide structure was useful because it allowed a great deal of structural variability to be built into the molecule.

Laboratory Colony and Field Evaluation

Twelve fluorinated sulfonamides (I, II, III, IV, VI, VII, VIII, IX, X, XXII, XXV, XXIV) were selected for evaluation against laboratory colonies of the fire ant. The materials were fed to queenright colonies formulated in soybean oil absorbed on a corn grit carrier (18). The queens in all colonies were either sick or dead by 21 days, and in most cases within 7 to 14 days. All of the compounds produced good delayed kill (1 to 24% after 2 to 3 days).

Although the laboratory colony results indicated that all the compounds warranted field tests, these tests are expensive, time consuming, and labor intensive (29), thus, other factors important to eventual commercialization, such as oil solubility, bait acceptance, and availability, were considered. Consequently, XXII, which was not very soluble in soybean oil and showed the lowest worker mortality was not tested. Compound X did not kill all of the queens in the four replicates and was also omitted.

Field assays of the 10 remaining compounds were conducted in Florida and Georgia. All chemicals were dissolved in once-refined soybean oil at concentrations of 1.0-2.5% (w/w). The oil solution was absorbed onto pregelled defatted corn grits 30% by weight of total formulation to yield baits containing 0.30, 0.60, or 0.75% active ingredient (AI). All baits were applied with a tractor-mounted auger applicator at 3.3, 4.9, or 8.1g AI/ha (29). Amdro fire ant bait (0.88% AI) was applied at the label recommendation rate of 10.4g AI/ha. Each treatment was replicated 3 times. Pretreatment and post-treatment evaluations were made at 6 and 12 wks. The pre-and post treatment population levels were used to calculate the percent control. Untreated plots similar in size to treated plots were monitored as controls.

The results demonstrated that several of the fluoro- aliphatic sulfones (I, II, III, XXV, and XXXIV) are suitable as bait-toxicants for control of the fire ant and have activity comparable to the currently available bait toxicant (Amdro).

Activity Against Other Insects

Social Insects. The same rationale for delayed-action toxicants against fire ants can be applied to other social insect pest species. Also, the potential for this class of compounds in the control of social insects is enhanced because their structural variety provides water and oil soluble compounds with a range of activities. Many of the compounds developed for fire ant control have been tested for efficacy against other ant pests (30,31) and several of the fluorinated sulfonamides were tested against the leaf-cutting ant, Acromyrmex octospinosus Reich. Four of these latter compounds (I, IV, VIII, and XXXVIII) showed excellent results in laboratory tests (Kermarrec, A., Centre de Recherches Agronomiques, Petit-Borg, Guadaloupe). Other social insect

pests such as, Pharoah's ants, the Argentine ant, the Formosan termite, and the Africanized honey bee, may be prime targets for this class of compounds.

Cockroaches, Mosquitoes and Houseflies. Initial tests against the American (Periplaneta americana) and German (Blattella germanica) cockroaches involved five fluorosulfonamides, (I, II, III, XIV, and XXII) that gave excellent delayed-action against the fire ant. The cockroach bait was composed of the toxicant formulated in a mixture of cornmeal and powdered sugar (32). For the American cockroach marked delayed activity was observed, with a mean mortality of only 5 percent after 24 hours. However, by 10 days all replicates had 100 percent mortality. In contrast, there was rapid mortality against the German cockroach (mean of 85 percent by the first day, 94 percent at day 2, and 100 percent by day seven). In both cases the trichlorfon standard gave 100 percent kill after 24 hours (25). In the control of cockroaches, delayed activity is not a necessary feature of potential control methods. Among the many fluorinated compounds tested several displayed rapid kill (IV, VIII, X, and XXV) and these compounds are currently being tested.

The same five fluorinated sulfonamides were screened as mosquito larvicides against Anopheles quadrimaculatus. Preliminary results showed that all of the compounds tested except XXII, had good to excellent larvicidal activity. Compound I compared well with the standard larvicide, temephos, with an LC-50 of 0.0029 ppm. In 24 hour mortality tests, all compounds except XXII gave 100 percent kill at 10 ppm and compound II gave 78 percent kill at 0.1 ppm (25). In the case of mosquito larvicide action, water solubility may be an important feature of the toxicant. Again the fluorinated sulfonic acids and their salts (XXXVIII and XXXIX) have greater water solubility. Tests with these compounds in the field have shown outstanding persistence and remarkable species selectivity (25; Roberts, R., USDA, Gainesville, Fl).

Compounds I, II, III, XIV, and XXII, were tested for insecticidal activity against houseflies (Musca domestica). The insecticide-resistant strain of housefly was fed a food bait containing 1 percent of the test compounds. After 3 days, compounds II, III, and XIV showed no mortality and compounds I and XXII gave only 80 and 60 percent mortality, respectively (25). As in the case of cockroaches, the faster acting analogues may provide a more acceptable level of control.

Conclusion

As illustrated in the previous discussion, this new class of insecticide was serendipitously discovered to have the very specialized delayed-activity over a wide range of concentrations required for fire ant control. These same properties may well broaden the use of these compounds to the control of other social insect pests. The wide range of chemical functional types, toxic activity and solubilities broaden the potential use of this class of compound to a wide variety of insect pests. Compound III is currently under commercial development by Griffin Corporation, Valdosta, Georgia, for fire ant control. If the compound passes the strict toxicological requirements of the EPA, the future of these chemicals for insect control will be very exciting.

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Chapter 22

Synthesis, Insecticidal Activity, and Anticholinesterase Activity of Some Oxadiazolones

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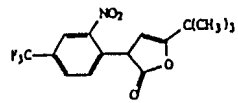
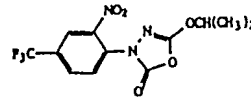
This report summarizes the synthesis, insecticidal activity, and anticholinesterase activity of some novel N-dihydrobenzofuranyl oxadiazolones. The compounds were primarily aphicides with reduced activity on houseflies, corn earworms and two-spotted spider mites. Some of these compounds were potent anticholinesterases (I_{50} values $1\text{-}10 \times 10^{-8}$ M) that were slowly reversible. There was little relationship between in vitro anticholinesterase activity and in vivo activity.

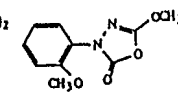
A synthesis program was initiated to optimize the insecticidal activity of the following molecules that are related to RP 32861, a substance reported to be insecticidal against sucking insects(1).



Housefly TI*=6



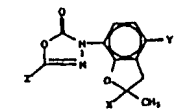
Aphid TI*=4



RP 32861

*Parathion TI=100

The new molecules had the following generalized structure(2):



Where X = H or CH_3
Y = H, halogen or alkyl
Z = alkoxy, aryloxy alkyl or aryl

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