on the long chain. The activity of compounds with methyl branching on the double-bonded carbon atoms of the long chain exhibited higher activity than compounds with a similar branch on the short chain. Thus, 10-methyl-9-docosene and 10-methyl-9-tricosene were much more active than 8-methyl-8-docosene and 9-methyl-9-tricosene.

The results of the pseudofly petri dish test showed a high degree of similarity (correlation coefficient 0.76) with those of olfactometer tests (Table IV). The few discrepancies (*e.g.*, 10-methyl-9-docosene ranked second in the olfactometer and thirteenth in the pseudofly test) did not negate the general agreement. The similarity of data derived by the two testing procedures on muscalure and its trans isomer was noted by Rogoff *et al.* (1973). Since the mating-type behavior elicited by muscalure and many of its analogs was accompanied by increased rates of capture (*i.e.*, greater attraction) in the olfactometer, our data are consistent with the hypothesis that muscalure is the compound that produced the sex stimulant and attractant action reported by Rogoff *et al.* (1964).

Structural requirements for activity of insect sex pheromones have been investigated only for a few insect species. Generally, any variation in structure causes a great loss in activity. In the case of muscalure, a number of structural variations have produced active compounds, some of which equal or even slightly exceed the activity of muscalure. Accordingly, requirements in chemical structure for activity of the muscalure molecule are not considered to be highly specific. This lower specificity may be characteristic of sex pheromones that, like muscalure, are not highly potent (*e.g.*, compared with the sex pheromones of many Lepidoptera).

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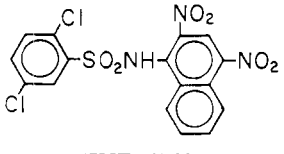
Insect Chemosterilants. Sulfonamides

Albert B. DeMilo,* Alexej B. Bořkovec, and Richard L. Fye

Seven *N*-(2,4-dinitro-1-naphthyl)benzenesulfonamides were more active as chemosterilants in *Musca domestica* L. (oral administration) than the 2,5-dichloro analog (ENT 52766) reported previously. As a male sterilant, 2,5-dichloro-2′,4′-dinitrobenzenesulfonanilide was ten times more effective than ENT 52766.

Most chemosterilants effective in male insects are biological alkylating agents but other classes of male chemosterilants have been discovered in the past 10 years (Bořkovec, 1972). When Fye *et al.* (1973) reported the activity of 2,5-dichloro-*N*-(2,4-dinitro-1-naphthyl)benzenesulfonamide (ENT 52766) in the male house fly, *Musca domesti-*



ENT 52766

ca L., no other structurally similar sulfonamide was known to sterilize male insects. Sterilants effective in both sexes are of special importance for practical application but a much higher activity than that shown by ENT 52766 would be desirable. Consequently, our efforts were directed toward synthesizing related sulfonamides with high sterilizing activity and toward determining which parts of the molecule exemplified by ENT 52766 were essential for activity. Herein we describe the results of this study.

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EXPERIMENTAL SECTION

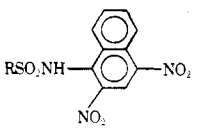
Synthesis of Chemicals. The melting points are uncorrected. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Tables of complete analytical data for the sulfonamides not mentioned in this section will appear in the microfilm edition; see paragraph at end of paper regarding supplementary material.

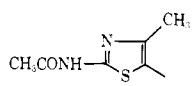
The majority of the *N*-(1-naphthyl)arylsulfonamide precursors were prepared by the procedure of Witt and Schmitt (1894). Alkylsulfonamides were prepared by condensing the appropriate sulfonyl chloride with 1-naphthylamine in pyridine solvent. Melting points of new compounds are listed in Table I.

N-(1-Naphthyl)aryl(or alkyl)sulfonamides were nitrated by a slightly modified method of Morgan and Godden (1910) and Morgan and Evens (1919). The general procedure which we have used for the preparation of a wide variety of *N*-(2,4-dinitro-1-naphthyl) derivatives, in yields ranging from 28 to 82%, follows.

N-(2,4-Dinitro-1-naphthyl)aryl(or alkyl)sulfonamides. To a solution or suspension of finely pulverized *N*-(1-naphthyl)aryl(or alkyl)sulfonamide (0.01 mol) in glacial acetic acid (20–30 ml) was rapidly added 70% nitric acid (0.021–0.022 mol). Usually the mixture was heated to 70–75° for 5–15 min but for exothermic reactions the initial temperature was allowed to subside prior to heating. In vigorous reactions, when the induction temperature exceeded 55°, no external heating was necessary. If the product did not precipitate during the reaction, cooling was used to induce

Table I. Chemosterilant Activities of *N*-(2,4-Dinitro-1-naphthyl)sulfonamides Fed to House Flies



ENT no.	R	Mp, °C[a]	Sterilizing act.[b]
62665	CH_3	189.5–191	0
62774	n-C_4H_9	144.5–146.5	0
62715	n-$C_{16}H_{33}$	106.5–108.5 (85–86)	0
62771	$C_6H_5CH{=}CH$	157.5–159	+
62758	p-$(CH_3O)C_6H_4$	167–169.5 (159–161)	+++
62586	p-$(CH_3)C_6H_4$	166.5–168.5[c]	+++
62583	C_6H_5	191–193[d]	+
62688	p-$(NHCOCH_3)C_6H_4$	210 dec	+++
62585	p-BrC_6H_4	219–221 dec	+++
62689	p-$(NO_2)C_6H_4$	211.5 dec	++
62821	o-$(NO_2)C_6H_4$	245–247 dec (171.5–173.5)	0
62822	m-$(NO_2)C_6H_4$	198–199.5[e]	0
52766	2,5-$Cl_2C_6H_3$	228.5–230 (186–188.5)	++
62756	3,4-$Cl_2C_6H_3$	179.5–180.5 (186–187.5)	+++
62684	2,3,4-$Cl_3C_6H_2$	172–173.5	+++
62714	2,4,5-$Cl_3C_6H_2$	207–209.5	+++
62757	2,5-$(CH_3)_2C_6H_3$	186–187.5 (142.5–144)	+
62690		190.5–192	0
62710		185–186 dec (186–188)	0
62787		238.5 dec (240.5–242.5)	0

[a] Data in parentheses are for the *N*-(1-naphthyl)sulfonamide precursors. [b] See Experimental Section for details. [c] Lit. mp 165–166° (Morgan and Evens, 1919). [d] Lit. mp 185–186° (Morgan and Godden, 1910). [e] Lit. mp 185–188° (Consden and Kenyon, 1935).

crystallization. The filtered product was recrystallized from ethanol or acetonitrile.

2,5-Dichloro-2',4'-dinitrobenzenesulfonanilide (*ENT 62775*). A mixture of the sodium salt of 2,5-dichlorobenzenesulfonamide (4.96 g) and 1-chloro-2,4-dinitrobenzene (2.02 g) in dimethylformamide (30 ml) was allowed to react for 1 hr. The solvent was removed *in vacuo* and the residue treated with water (50 ml) to precipitate a yellow solid. The solid was triturated with 5% acetic acid (50 ml), recollected by filtration, and recrystallized from ethanol to give 1.70 g (44%) of ENT 62775, mp 147–150°. An analytical sample had a mp of 152–154°.

Anal. Calcd for $C_{12}H_7Cl_2N_3O_6S$: C, 36.75; H, 1.80; N, 10.73. Found: C, 36.70; H, 1.70; N, 10.61.

2,5-Dichloro-2',4',6'-trinitrobenzenesulfonanilide (*ENT 62785*). This material was prepared similarly to ENT 62775 with picryl chloride as the active halide. Evaporation of the solvent gave an oily residue that crystallized when treated with water. Then the aqueous suspension was warmed (*ca.* 40–45°) and the insoluble 2,5-dichlorobenzenesulfonamide was removed by filtration. Acidification of the filtrate precipitated the crude product. Recrystallization from acetonitrile gave ENT 62785, mp 210–211.5°, in a 69% yield.

Anal. Calcd for $C_{12}H_6Cl_2N_4O_8S$: C, 32.96; H, 1.38; N, 12.82; Cl, 16.22. Found: C, 32.91; H, 1.60; N, 12.61; Cl, 16.21.

2,5-Dichloro-α,α,α-trifluoro-2',6'-dinitrobenzenesulfono-p-toluidide (*ENT 62786*). In a procedure similar to that used for ENT 62785, 4-chloro-α,α,α-trifluoro-3,5-dinitrotoluene (Hall and Giam, 1972) was used as the active halide and ENT 62786, mp 138.5–141°, was obtained in a 76% yield.

Anal. Calcd for $C_{13}H_6Cl_2F_3N_3O_6S$: C, 33.91; H, 1.31; N, 9.13. Found: C, 34.09; H, 1.35; N, 9.21.

2,5-Dichloro-N-(2-nitro-1-naphthyl)benzenesulfonamide (*ENT 62788*). Treatment of the sodium salt of 2,5-dichlorobenzenesulfonamide with 1-chloro-2-nitronaphthalene (Hoogeveen, 1931) at 90° for 2.5 hr in dimethylformamide gave ENT 62788, after similar work-up used for ENT 62785. Recrystallization of the product from ethanol gave yellow plates (53%), mp 189–194.5°.

Anal. Calcd for $C_{16}H_{10}Cl_2N_2O_4S$: C, 48.39; H, 2.54; N, 7.05; Cl, 17.85; S, 8.07. Found: C, 48.45; H, 2.43; N, 7.06; Cl, 17.74; S, 8.17.

2,5-Dichloro-N-(4-nitro-1-naphthyl)benzenesulfonamide (*ENT 62664*). Treatment of 1-amino-4-nitronaphthalene (8.90 g) with 2,5-dichlorobenzenesulfonyl chloride (11.60 g) in pyridine (50 ml) for 2 hr at 25° gave, after work-up and recrystallization from acetonitrile, 7.40 g (53%) of pure ENT 62664, mp 241.5° dec.

Anal. Calcd for $C_{16}H_{10}Cl_2N_2O_4S$: C, 48.39; H, 2.54; N, 7.05. Found: C, 48.26; H, 2.64; N, 6.90.

2,5-Dichloro-N-(2,4-dinitro-1-naphthyl)-N-methylbenzenesulfonamide (*ENT 62697*). In a similar procedure to that used for ENT 62785, the sodium salt of 2,5-dichloro-*N*-methylbenzenesulfonamide was treated with 1 equiv of 1-chloro-2,4-dinitronaphthalene. Evaporation of the solvent gave a syrupy residue that crystallized when triturated with ethanol. Recrystallization from acetonitrile gave pure ENT 62697 (33%), mp 201.5–203°.

Anal. Calcd for $C_{17}H_{11}Cl_2N_3O_6S$: C, 44.75; H, 2.43; N, 9.21; S, 7.03. Found: C, 44.86; H, 2.37; N, 9.38; S, 7.14.

Biological Tests. Details of the procedure were described previously (Fye *et al.*, 1966). Briefly, each compound was added on a w/w basis to a diet of sucrose, nonfat dry milk, and powdered egg yolk (6:6:1). Flies that were kept on the medicated diet were allowed to mate and their reproductive performance was evaluated and compared with that of control flies. To assess the effects on males, the treated males were crossed with virgin untreated females and the fertility of the mated females was again evaluated. The sterilizing activity of a compound was classified as high (+++) when full sterility was induced with diets containing less than 0.025% of the agent, moderate (++) when the concentration was 0.025–0.1%, and low (+) when the concentration was 0.25–1.0%. Compounds that induced less than 50% sterility at 1% concentration were considered inactive (0).

RESULTS AND DISCUSSION

Considering the structure of ENT 52766, we initially decided to determine the sterilizing activity of its four potential hydrolysis products, since hydrolytic cleavage of the sterilant might occur during digestion. Hence, 2,5-dichlorobenzenesulfonic acid, 2,4-dinitro-1-naphthylamine, 2,5-dichlorobenzenesulfonamide, and 2,4-dinitro-1-naphthol were tested but all were inactive.

Our first modification of ENT 52766 was restricted to the dichlorophenyl portion of the molecule and, as Table I shows, seven of these derivatives were more active than the original compound. Replacement of the 2,5-dichlorophenyl moiety with alkyl groups (ENT 62665, ENT 62774, ENT 62715), or with aryl groups other than phenyl or substituted phenyl (ENT 62690, ENT 62710, ENT 62787), led

to inactive compounds. A series of phenyl derivatives containing various electron-donating or -withdrawing substituents in the 4 position was prepared to evaluate the electronic contribution to the sterilizing properties of the molecule. However, a comparison of the activities of ENT 62758 and ENT 62586 to those of ENT 62585 and ENT 62689 plainly indicated that changes in electronic effects were not related to the activity of the sulfonamides.

Selected groups of compounds, designed to correlate changes in activity with changes in location of various substituents on the benzene ring, gave conflicting results. For example, in the two isomeric pairs of chloro-substituted derivatives (ENT 52766, ENT 62756 and ENT 62684, ENT 62714) each isomer in a pair had essentially the same sterilizing activity. However, in the nitrobenzene series, the ortho (ENT 62821) and meta (ENT 62822) isomers were inactive whereas the para isomer (ENT 62689) was moderately active.

The second modification of ENT 52766 concerned the naphthyl portion of the molecule. Inactive compounds resulted from eliminating one of the two nitro groups (ENT 62664, ENT 62788), but when the entire 2,4-dinitro-1-naphthyl group was replaced with the 2,4-dinitrophenyl group (ENT 62775), moderate activity was obtained when both sexes were treated, and male sterility increased about tenfold. However, addition of another nitro substituent to the benzene ring (ENT 62785) gave a highly toxic picryl derivative with no apparent sterilizing activity. Similar results were encountered for ENT 62786, a trifluoromethyl analog of ENT 62785.

The importance of an unsubstituted amidic nitrogen as a prerequisite for activity became apparent when methylation of the nitrogen in ENT 52766 gave inactive ENT 62697 and replacement of the amidic function in ENT 62586 with oxygen gave the inactive 2,4-dinitro-1-naphthol-*p*-toluenesulfonate.

Because of the important role that male chemosterilants may play in the sterile-male technique of insect control, further investigation of the sulfonamides related to ENT 52766 should be directed toward the naphthyl substituent, particularly to its replacement with various substituted phenyl or other groups.

Supplementary Material Available. A listing of structure factor amplitudes will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N. W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JAFC-74-197.

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Photochemistry of Bioactive Compounds: Photoproducts and Kinetics of Polychlorinated Biphenyls

Luis O. Ruzo, Matthew J. Zabik,* and Robert D. Schuetz

Several symmetric tetrachlorobiphenyls were synthesized by modified Ullmann coupling of the corresponding dichloroiodobenzenes. Hexane and methanol solutions of these compounds were irradiated at 300 nm for different time periods and the photoproducts analyzed by gas chromatography and mass spectrometry. In hexane only, dechlorination products were observed, while in methanol solution additional methoxylated products were formed. Photoreaction rates have been measured and a marked difference in reactivity has been observed for tetrachlorinated biphenyls with chlorine substituents in different positions on the aromatic rings. Mechanistic pathways for this reaction consistent with our observations are discussed.

Ultraviolet radiation is known to induce chemical reactions in many chlorinated hydrocarbons under laboratory conditions (Mitchell, 1961). Some of these reactions have also been found to occur under field conditions (Crosby and Tutass, 1966). Identification of the resulting photoproducts and investigation of their chemical, toxicological, and pharmacological properties are necessary in order to have a correct evaluation of the merits involved in their continued use.

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Polychlorinated biphenyls (PCB) are among those compounds which have received considerable attention in recent years. They have been found to occur together with chlorinated pesticides in human adipose tissue and milk (Acker and Schulte, 1970; Biros *et al.*, 1970). Several reviews have appeared describing their chemical and toxicological properties (Edwards, 1971; Vos, 1970). It is generally agreed that their presence in the environment and in foods is detrimental.

We have undertaken the study of PCB photochemistry in order to determine the structure of the resulting photoproducts, the effect of solvents on product formation and rates of reaction, and any correlations between PCB structure and their rate of photolysis.