



R57-11

## The Evaluation of Triethyl Tin Hydroxide and its Esters as Insecticides<sup>1</sup>

MURRAY S. BLUM and FRANK A. BOWER, *Chemicals and Plastics Division, Quartermaster Research and Development Center, Natick, Massachusetts*

The toxic properties of organotin compounds were first described by White (1886), who found that triethyl tin acetate, in contrast to inorganic tin salts, was highly toxic to dogs, rabbits and frogs. Kerk & Luitjen (1954) reported a similar effect in studies of the fungicidal activity of certain heavy metal compounds. Mercury, copper, zinc and cadmium were found to be fungicidal in the ionic state while ionic tin was non-toxic to fungi. Certain organotin compounds, however, were found to be highly toxic. This property of being essentially non-toxic in the ionic state and highly toxic in the non-ionic form, gives tin a unique place among the heavy metals.

Until recently, possible uses for organotin compounds had received little consideration. The use of tetra-alkyl and tetra-aryl tin compounds as moth-proofing agents was claimed in a patent granted to I. G. Farbenindustrie A.-G. (1929a). Later patents (I. G. Farbenindustrie 1929b, Hartmann *et al.* 1930a, 1930b) claimed as effective moth-proofing agents all organic compounds of quadrivalent tin having one atom of tin per molecule. A more recent patent (N. V. de Bataafsche Petroleum Maatschappij 1943) claimed the use of triethyl tin chlorides in insect sprays.

In this laboratory, triethyl tin hydroxide was found to have a high degree of toxicity to house flies. In order to evaluate further the toxicity of organotin compounds and to study in greater detail some derivatives of triethyl tin hydroxide, a number of esters of triethyl tin hydroxide and various alkyl and aryl organic acids, prepared as part of the elastomer research program at this Center, were studied. Several esters including the triethyl tin ester of chrysanthemum monocarboxylic acid (a hydrolysis product of pyrethrum) and the ester of bis-(*p*-chlorophenyl) acetic acid (a possible degradation product of bis-(*p*-chlorophenyl) methyl carbinol from its metabolism by certain insects) were prepared specifically for this investigation.

**METHODS AND MATERIALS.**—*Preparation of triethyl tin esters.*—The triethyl tin esters used in this study were prepared by the reaction of triethyl tin hydroxide and the desired acid or its anhydride. The reactions were very rapid, being completed as soon as the reactants were brought into solution. When liquid acids were employed, a solvent was unnecessary. Warming the mixture of organic acid and triethyl tin hydroxide followed by re-

Table I.—Preparation and properties of triethyl tin esters.

TRIETHYL TIN COMPOUND	SOLVENT	MELTING POINT (° C.)	ANALYSIS		YIELD (PER CENT)
			Calculated	Found	
Formate	None	55-57	— <sup>a</sup>	—	76
Acetate	None	130.5-131	— <sup>b</sup>	—	60
Acrylate	Ethanol	111-112	C—39.01 H— 6.50	C—38.88 H— 6.60	100
Benzoate	Ethanol	73-75	C—47.73 H— 6.12	C—47.59 H— 6.42	70
(bis- <i>p</i> -Chlorophenyl) acetate	Ethanol	112-113	C—49.45 H— 4.95	C—49.50 H— 5.17	93
<i>d</i> -trans-Chrysantheumate	None	129-129.5	C—51.52 H— 8.05	C—51.23 H— 8.29	100

<sup>a</sup> Previously reported; Cahours (1860).

<sup>b</sup> Previously reported; Nesmeyanov *et al.* (1937).

crystallization gave good yields of pure crystalline compound. Reactions involving solid acids were carried out in alcoholic solution and the resulting esters were isolated by precipitation with water. Recrystallization from ethanol-water or petroleum ether gave pure samples of these esters. One example of each technique is given in detail below and the remainder are summarized in table 1.

*Triethyl tin acetate.*—Triethyl tin hydroxide (0.56 gm., 0.0025 mol.), 3 ml. of acetic anhydride and one drop of pyridine were mixed in a 25 ml. flask fitted with a reflux condenser. The solution was warmed gently to initiate the reaction. After the initial spontaneous reaction had subsided, the mixture was refluxed for 20 minutes and allowed to stand overnight. The white crystalline precipitate was separated by filtration and washed with cold petroleum ether giving 0.40 gm. (60%) of triethyl tin acetate, m.p. 130.5-131.0° C.; lit. m.p. 130-131° C. (Nesmeyanov *et al.* 1937).

*Triethyl tin benzoate.*—Triethyl tin hydroxide (0.485 gm., 0.0022 mol.) and 0.266 gm. (0.0022 mol.) of benzoic acid were dissolved in 5 ml. of ethanol and heated to boiling. An equal amount of water was added and the mixture cooled. An oil separated which crystallized on standing to give 0.5 gm. of crude triethyl tin benzoate. Recrystallization from cold petroleum ether gave 0.3

<sup>1</sup> Accepted for publication August 14, 1956.

<sup>2</sup> The authors wish to thank Dr. H. H. Moorefield of Union Carbide and Carbon Corp., Yonkers, N. Y., for this evaluation.

Table 2.—Toxicity of triethyl tin hydroxide and six of its esters toward DDT-susceptible (S) and resistant (R) house flies.

TRIETHYL TIN COMPOUND	DOSE ( $\mu$ G.) PER FLY	PER CENT MORTALITY		LD <sub>50</sub> ( $\mu$ G./FLY)	
		S	R	S	R
Hydroxide	0.10	20	10	0.31	0.40
	.25	45	30		
	.50	70	55		
	.75	100	80		
Formate	0.10	35	5	0.25	0.45
	.25	50	25		
	.50	70	55		
	.75	95	90		
Acetate	0.10	15	15	0.30	0.54
	.25	40	25		
	.50	90	45		
	.75	100	75		
Acrylate	0.10	10	—	0.42	0.70
	.25	30	20		
	.50	70	35		
	.75	95	60		
	1.00	—	95		
Benzoate	0.25	10	—	0.52	0.74
	.50	35	20		
	.75	70	55		
	1.00	90	75		
	1.50	—	100		
<i>d-trans</i> Chrysan- themumate	0.25	15	—	0.51	0.93
	.50	45	15		
	.75	75	35		
	1.00	100	55		
	1.50	—	90		
bis( <i>p</i> -Chlorophenyl) acetate	0.50	20	—	0.76	1.28
	.75	35	15		
	1.00	65	35		
	1.50	95	60		
	2.00	—	85		

gm. of pure triethyl tin benzoate, m.p. 73–75° C. Anal. Calcd. for C<sub>12</sub>H<sub>20</sub>O<sub>2</sub>Sn: C-47.73; H-6.13. Found: C-47.59; H-6.42.

For the purposes of this study, the various esters and the parent base were evaluated biologically as dilute solutions in redistilled acetone.

House flies used in this investigation were the susceptible Chemical Specialties Manufacturers Association strain and the DDT-resistant Orlando-Beltsville strain. The larvae were reared on moist Purina dog pellets at 30° C.

Twenty adults of both sexes, 3 to 4 days old, were lightly anesthetized with carbon dioxide and treated topically with 1 microliter of a dilute (0.01–0.2%) solution of the compound in acetone. Controls demonstrated that this quantity of acetone was non-toxic to house flies. The solution was administered from a 0.25 ml. tuberculin syringe, the plunger of which was driven with a micrometer. Two duplicates of four replicates at each dosage were run on each compound tested. After treatment, each group of 20 flies was kept in a half-pint Mason jar at 30° C. for 24 hours, at which time a mortality count was made. A suspension of powdered milk was supplied to the flies for this period.

RESULTS AND DISCUSSION.—As the data in table 2 demonstrate, triethyl tin hydroxide and its esters were toxic to susceptible and DDT-resistant strains of house flies. All the compounds were slightly more toxic to the susceptible than to the resistant strain. The LD<sub>50</sub> values for triethyl tin hydroxide and its six esters for DDT-resistant and susceptible house flies are given in table 2.

Since the parent compound, triethyl tin hydroxide, was at least as toxic as any of the compounds tested, and the esters showed a decreasing toxicity with increasing molecular weight, it would appear that the toxic moiety is the triethyl tin portion of the molecule.

Triethyl tin hydroxide and its esters quickly produced paralysis in house flies. At higher dosages the flies seemed to recover from anesthesia, as evidenced by leg movements, but remained prostrate until death occurred. This phenomenon may have been the result of the overlapping independent actions of carbon dioxide and the insecticide or the result of an interaction between the two compounds. Although no definitive experiments were performed, it is felt that the paralytic effect was due to the organotin compound alone.

Examination of the triethyl tin esters as anticholinesterases demonstrated that these materials do not inhibit this enzyme at concentrations up to  $1 \times 10^{-3}$  molar<sup>2</sup>. However, it was determined that these esters are capable of blocking the spontaneous activity of the isolated central nerve of the American cockroach (*Periplaneta americana* (L.))<sup>3</sup>. Aldridge & Cremer (1955) have shown that triethyl tin sulfate inhibits phosphorylation processes associated with oxidation in the rat brain and liver mitochondria.

These observations support the assumption that the triethyl tin derivatives were responsible for the rapid paralysis observed in the insect. They also offer some insight into their mode of action.

SUMMARY.—The toxicity of triethyl tin hydroxide and its formate, acetate, acrylate, benzoate, bis(*p*-chlorophenyl) acetate and *d-trans*-chrysanthemumate esters have been investigated. All were found to induce paralysis quickly and to cause death at a very low dosage level. These compounds were somewhat more toxic to susceptible flies than to DDT-resistant flies.

Triethyl tin esters were found to be ineffective as inhibitors of cholinesterase. However, conduction in the isolated nerve cord of the American cockroach was completely blocked by these esters.

#### REFERENCES CITED

- Aldridge, W. N., and J. E. Cremer. 1955. The biochemistry of organotin compounds. Diethyl tin dichloride and triethyl tin sulfate. *Biochem. Jour.* 61: 406–18.
- Cahours, A. 1860. Untersuchungen über die metallhaltigen organischen Radicale. *Ann.* 114: 354–82.
- Hartmann, E., M. Hardtmann, and P. Kummel. 1930a. U. S. Patent 1,744,633.
- Hartmann, E., P. Kummel, and M. Hardtmann. 1930b. Ger. Patent 485,646.
- I. G. Farbenindustrie A. -G. 1929a. Dutch Patent 20,570.
- I. G. Farbenindustrie A. -G. 1929b. Brit. Patent 303,092.
- Kerk, G. J. M. van der, and J. G. A. Luitjen. 1954. Investigations on organotin compounds, III. The biocidal

The authors wish to thank Dr. G. F. Shambaugh for these determinations.

- properties of organotin compounds. Jour. Appl. Chem. 4: 314-19.
- Nesmeyanov, A. N., K. A. Kocheshkov, and V. P. Puzyreva. 1937. Reduction of organic mercury compounds by aliphatic tin compounds as a synthetic method for aromatic stannanes substituted in the nucleus with hydroxy and amino groups. Jour. Gen. Chem. (U.S.S.R.) 7: 118-21. (C. A. 31: 42907).
- N. V. de Bataafsche Petroleum Maatschappij. 1943. Dutch Patent 68,578.
- White, T. P. 1886. The action of tin on the animal organism. Pharm. Jour. 17: 166-8.

Reprinted from the  
JOURNAL OF ECONOMIC ENTOMOLOGY  
Vol. 50, No. 1, pp. 84-86, February, 1957