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Some Physical, Chemical, and Insecticidal Properties of Some *O,O*-Dialkyl *O*-(3,5,6-Trichloro-2-Pyridyl) Phosphates and Phosphorothioates

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Large differences have been observed between the physical, chemical, and insecticidal properties of four representatives of a closely related series of O,O-*dialkyl* O-*(3,5,6-trichloro-2-pyridyl) phosphates and phosphorothioates. These differences are important in explaining large variations in the persistence of the compounds and in their toxicity for insects that arise from the use of different test methods and formulations, representing various uses of the insecticides.*

For purposes of prediction and for a better understanding of the means of distribution of insecticides in the environment and of their toxicities to different organisms, it is helpful to compare the results of different insecticide tests with the physical and chemical properties of the compounds concerned.

The following compounds were selected for study: (1) DOWCO 179, *O,O*-diethyl *O*-(3,5,6-trichloro-2-pyridyl) phosphorothioate, the active ingredient of Dursban insecticide; (2) DOWCO 180, 3,5,6,-trichloro-2-pyridyl diethyl phosphate; (3) DOWCO 214, *O,O*-dimethyl *O*-(3,5,6-trichloro-2-pyridyl) phosphorothioate; and (4) DOWCO 217, 3,5,6-trichloro-2-pyridyl dimethyl phosphate.

STRUCTURE AND PHYSICAL AND CHEMICAL PROPERTIES

The structure of the four compounds is shown in Table 1, and some of their physical and chemical properties are listed in Table 2. These properties—such as vapour pressure, solubility, partition coefficient, and hydrolytic stability at various pH values—are those that appear to be critical for correlation with insecticidal activity.

Of the four compounds in this series, the phosphates and phosphorothioates show greater variations in physical and chemical properties than do the methyl and ethyl esters (Table 2). The phosphorothioates have much higher vapour pressures, higher *n*-octanol/water partition coefficients, and greater hydrolytic stabilities in water–methanol solutions and are much less soluble in water than their respective phosphate analogues. Although the differences are less significant, the ethyl esters have lower vapour pressures, lower solubilities in water, and greater hydrolytic stabilities than their respective methyl homologues.

The rates of hydrolysis of the four compounds were determined in buffered water-methanol solutions at different pH values and after various time intervals. The hydrolysis of 3,5,6-trichloro-2-pyridinol was measured by means of ultraviolet spectrum analysis, and a constant was calculated by the use of the equation

$$K = (2.303/t) \times c/(c-x)$$

where t is time, c the initial concentration, and x the amount hydrolysed. When log K is plotted against time and the line is extrapolated to zero time, a straight line is obtained in the absence of important side-reactions. The curves thus obtained for the four compounds under discussion show considerable differences. For DOWCO 179 and 180, straight lines are obtained, indicating that the principal product of hydrolysis is 3,5,6-trichloro-2-pyridinol. With DOWCO 214, however, curved lines are obtained at pH 4, pH 6, and pH 8, indicating that one or both of the methyl-ester bonds may be undergoing simultaneous hydrolysis and that this may, in fact, be the principal reaction. Demethylation of DOWCO 217 probably occurs at about the same rate as that of DOWCO 214, but hydrolysis to the

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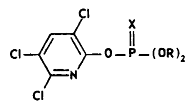
Table 1
Structure of the four
O,O-dialkyl *O*-(3,5,6-trichloro-2-pyridyl)
phosphates and phosphorothioates

GENERAL FORMULA



DOWCO 179	DOWCO 180	DOWCO 214	DOWCO 217
X = S R = C_2H_5	X = O R = C_2H_5	X = S R = CH_3	X = O R = CH_3

pyridinol proceeds so much more rapidly with the former compound that demethylation is not detected by the test method.

Differences in the speed or selectivity with which the four compounds are demethylated and/or hydrolysed to the pyridinol may form a basis for selective toxicity for different phylla and species.

CORRELATION WITH TOXICITY TO INSECTS

The biological activity of the four compounds is related to their physical and chemical properties. This is illustrated by the results of different insecticide tests. The toxicity data presented in Tables 3 and 4 were obtained by the use of test methods described by Kenaga et al. (1965). These methods involve the use of the chemicals in acetone, aqueous emulsions,

Table 2
Some properties of the four *O,O*-dialkyl *O*-(3,5,6-trichloro-2-pyridyl) phosphates and phosphorothioates and of DDT

Property	DOWCO 179 [a]	DOWCO 180 [b]	DOWCO 214 [b]	DOWCO 217 [b]	DDT [c]
Molecular weight	350.5	334.5	322.5	306.5	354.4
Melting point (°C)	42–43.5	44–45	45.6–46.5	92.3	109
Vapour pressure at 25°C (mmHg × 10^{-5})	1.87	—	4.22	0.42	0.03
Solubility in water at 23–25°C (ppm)	0.4	520 (?)	4.0	300 (?)	0.001
Solubility in organic solvents at 23°C (g/100 g)					
acetone	650	1 090	640	51	74
benzene	790	680	520	48	89
chloroform	630	530	350	85	29
ethanol	63	—	30	20	5
methanol	45	1 350	—	—	—
n-octanol	> 33	> 160	20	5.6	—
Partition coefficient, *n*-octanol/water [e]	66 600	1 520	9 300	—	—
Hydrolysis in 50 % v/v methanol/water solution at 23°C: half-life (days) at the following pH values:					
pH = 5	1 100	> 85	10	5.3 [d]	—
pH = 6	1 600	—	40	—	—
pH = 7	350	6.3	—	0.63 [d]	—
pH = 8	55	—	3	—	—
pH = 9	30	0.71	<3	0.63 [d]	—

[a] Data of Brust (1966).
[b] Unpublished data, The Dow Chemical Company, 1971.
[c] Data of Bowman et al. (1960) and of Brown (1951).
[d] Half-life in 25 % v/v methanol/water solution.
[e] Data of Hansch (1964).

oil, and dust formulations in order to compare their vapour, contact, and residual toxicity to insects.

Results of the most basic contact toxicity test are given in Tables 3 and 4 in the form of topical LD_{95} values for the housefly, *Musca domestica* L., and the American cockroach, *Periplaneta americana* (L.). This direct topical test shows DOWCO 179 and 214 to be equally toxic to the housefly. A comparison of the vapour pressures of these two compounds shows the volatility of DOWCO 214 to be 2–3 times that of DOWCO 179. This property is reflected in the housefly bioassay results, where the vapour-transfer toxicity of DOWCO 214 is seen to be 3 times that of DOWCO 179, and in the results of the treated-panel residual-toxicity test, which show DOWCO 179 to have 3 times the persistence of DOWCO 214 in contact action. From the results of the topical-application and dust tests, the four compounds may be listed, in order of decreasing toxicity to the American cockroach, as follows: DOWCO 180, DOWCO 217, DOWCO 179, and DOWCO 214 (Table 4). The results of the water-immersion test give the order DOWCO 180, DOWCO 179, DOWCO 217, and DOWCO 214. The change in the position of DOWCO 217 in the results of the immersion test may reflect its relative hydrolytic instability, and this is supported by the results of the topical-application and water-immersion tests (Table 3), which show that the toxicity of the two phosphates to the housefly relative to that of the two phosphorothioates is much lower in the water-immersion test than in the topical-application test.

Table 3

Relative toxicity of the four compounds to the adult housefly, using different test methods *

Compound	Topical application [a] LD_{95} (μg/insect)	Water immersion [b] LC_{95} (ppm)	Vapour [c] KD_{95} (min)	Duration of 95% mortality [d]
DOWCO 179	0.075	6.6	250	12
DOWCO 180	0.182	43.0	900	0.1
DOWCO 214	0.075	6.6	85	4
DOWCO 217	0.240	56.0	900	0

* Kenaga, E. E. & Whitney, W. K., unpublished data, 1966; Kenaga et al. (1965); Rigterink & Kenaga (1966). Mortality counts were made after 24-h exposures.

[a] Topical application of a solution in acetone to the thorax of the female fly.

[b] The insects were momentarily immersed in a water emulsion.

[c] Both males and females were held in untreated jars of 1 US gal capacity (about 3.8 litres), which were connected to jars of 1 US pint capacity (about 0.47 litre). The inner walls of the smaller jars were treated with the compounds at a level of 100 mg/ft^2 (about 1.075 g/m^2).

[d] Male and female flies were permitted to alight on a fir plywood panel, treated with insecticide at 40 mg/ft^2 (approximately 150 mg/m^2), that was hung, for 24-h periods, inside an untreated wide-screen cage at various intervals of time after the application of the insecticide. The figures in the column show the time in weeks (i.e., the time after the treatment of the panel) at the end of which 95% mortality was still obtainable.

Table 4

Relative toxicity of the four compounds to the cockroach, using different test methods *

Compound	*Periplaneta americana* (nymph)			*Blattella germanica* (adult male)	
	Topical application [a] LD_{95} (μg/insect)	Water immersion [b] LC_{95} (ppm)	Dust [c] KD_{95} (min)	Oil spray [d] LC_{95} (g/100 ml)	Dust [c] KD_{95} (min)
DOWCO 179	1.1	26	250	0.085	1 230
DOWCO 180	0.38	12	40	0.026	40
DOWCO 214	2.05	110	430	0.046	560
DOWCO 217	0.62	60	72	0.041	45

* Kenaga, E. E. & Whitney, W. K., unpublished data, 1966; Kenaga et al. (1965); Rigterink & Kenaga (1966). Mortality counts were made after 24-h exposures.

[a] Topical application of a droplet of solution in acetone on the thorax.

[b] The insect was momentarily immersed in a water emulsion.

[c] The insect was exposed to a 2 % dust formulation (2 mg of active ingredient per ft^2).

[d] Chemical Specialties Manufacturers Association (CSMA) oil-spray test method.

The partition coefficient has an important influence on the extent to which a compound penetrates and is distributed in the fat tissues of plants and animals, especially if the compound is not easily hydrolysed or metabolized. The data presented in this paper and the known rates of metabolism of DOWCO 179 (Smith, 1966; Smith et al., 1967) lead to the view that it is unlikely that the four compounds discussed herein are sufficiently stable to accumulate in fat tissues, in spite of the high *n*-octanol/water partition coefficient of DOWCO 179.

A unique property of the two phosphate compounds is their quick knock-down effect on cockroaches (Whitney et al., 1969) and other insects. It appears that this effect results from an ideal combination of physical, chemical, and biological properties that enables these compounds to penetrate quickly to the critical site in the insect.

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