

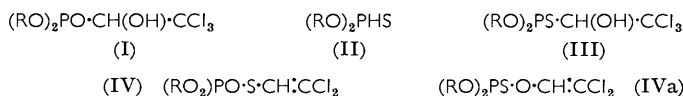
45. Studies on Organic Phosphorus Compounds. Part II.* Dialkyl Phosphorothioites and Their Reaction with Chloral.

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The reaction of dialkyl phosphorothioites with chloral is accompanied by rearrangement and dehydrohalogenation and yields *OO*-dialkyl *S*-(2,2-dichlorovinyl) phosphorothioates (IV). The structures of the starting materials and the products are discussed on the basis of their infrared spectra and molecular refraction. The effect of the compounds (IV) on mice and flies has been investigated.

DIALKYL PHOSPHITES react with chloral to give compounds (I), which are valuable insecticides.¹ It seemed of interest to study the corresponding reaction of dialkyl phosphorothioites (II), which can be prepared by reaction of dialkyl phosphorochloridites $(RO)_2PCl$ with hydrogen sulphide in the presence of a tertiary base² or by reaction of a suitable alcohol with phosphorus trisulphide (P_4S_6) .³ Reaction of the thioesters (II) with chloral did not give the expected compounds (III) but was accompanied by rearrangement and dehydrohalogenation, yielding *OO*-dialkyl *S*-(2,2-dichlorovinyl) phosphorothioates (IV).

The analogous reaction of compounds (I) takes place only when they are treated with an alkaline reagent. If the two rearrangements are analogous, the hydroxyl-oxygen atom of (I) will appear in the rearranged product in the P=O grouping. The structure of the compounds (II) and (IV) follows from the molecular refraction and the infrared spectrum.



The P=S double bond, which in $PSCl_3$ has been found to have a very broad band with its centre at 754 cm^{-1} and a frequency⁵ between 535 and 745 cm^{-1} , appears also in the infrared spectra of dimethyl, diethyl, and dipropyl phosphorothioite; these spectra do not contain the bands (2550 — 2600 cm^{-1}) characteristic of the S-H stretching vibration,⁶ but show the very distinct P-H bands⁶ at 2400 cm^{-1} and the P-O-C vibration⁷ around 1000 cm^{-1} . The structure of the dialkyl phosphorothioites (II) is, therefore, analogous to that of the dialkyl phosphites.⁸

In the infrared spectrum of the condensation products (IV) the following bands have been observed: (IV; R = Me) 3550 , 3100 , 3000 , 2900 , 1560 , 1450 , *1270*, *1185*, *1025* (broad), *915*, *825*, *795*, *655* (italics denote strong bands); (IV; R = Et) 3000 , 1560 , (1475), 1450 , 1390 , *1270*, 1160 , *1000* (very broad), *915*, 810 (broad), *655*; (IV; R = Prⁿ) 3000 , 1525 , 1470 , 1390 , *1270*, 1150 , *1000* (broad), *915*, 855 , 815 , 745 , *655*.

Whilst the P=S band is absent, all the spectra exhibit the characteristic vibration of the P=O bond (1270 cm^{-1}). The bands in the 1400 — 1560 region are due to the C=C double bond, and the broad bands around 1000 cm^{-1} to the P-O-C vibration. The band

* Part I, preceding paper.

¹ Lorenz, Henglein, and Schrader, *J. Amer. Chem. Soc.*, 1955, **77**, 2554; Zbirovsky and Ettel, *Sbornik vysoke školy chem.-technol v Prase*, 1957, 253 (*Chem. Abs.*, 1959, **53**, 6057).

² Sallman, U.S.P. 2,805,241 (*Chem. Abs.*, 1958, **52**, 2048).

³ Kabachnik and Mastryukova, *Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk*, 1952, 727.

⁴ Barthel, Alexander, Giang, and Hall, *J. Amer. Chem. Soc.*, 1955, **77**, 2424.

⁵ Hooge and Christen, *Rec. Trav. chim.*, 1958, **77**, 911.

⁶ Jones and Sandorfy, "Chemical Applications of Spectroscopy," in "Technique of Organic Chemistry," Interscience Publ. Inc., New York, 1956, Vol. VIII, p. 247.

⁷ Bergmann, Littauer, and Pinchas, *J.*, 1952, 847.

⁸ Daasch, *J. Amer. Chem. Soc.*, 1958, **80**, 5301; Kabachnik and Mastryukova, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1953, 163 (*Chem. Abs.*, 1954, **48**, 3243). This has recently been confirmed by measurements of the nuclear magnetic resonance (Yamasaki, *Sci. Reports Res. Inst. Tohoku Univ.*, Ser. A, 1959, **11**, 73).

at 655 cm^{-1} may be assigned to the S-C stretching vibration.⁹ The absence of the P=S frequency precludes formula (IVa) which would be as compatible as (IV) with the observed values for the molecular refraction (see Table 3).

Biological tests with the compounds of formula (IV) were carried out with male, white mice and with flies, both a susceptible and a D.D.T.-resistant strain of *Musca vicina* Macq. Quantities of the order of LD_{50} diluted with saline and injected into white mice produced after 7–10 min. the symptoms of cholinesterase poisoning (tremors, salivation, lachrymation, convulsions, and dyspnoea), followed by coma and death. Blood and brain of animals poisoned with 2 LD_{50} were tested for cholinesterase (ChE); the results are summarised in Table 1.¹⁰ The method used in the fly tests has been described by Tahori.¹¹ Benzene solutions of the compounds were applied topically to groups of 25 houseflies, and

TABLE 1. *Toxicity of compounds (IV).*

R	LD_{50} (mg./kg.)	Time of death (min.)	Mice		Flies, insecticidal activity (mg./fly)	
			% of residual ChE blood	brain	Susceptible	Resistant
Me	83	10–40	45–74	60–100	0.08	0.12
Et	30.6	10–20	46–55	40–50	0.03	0.04
Pr ⁿ	80	30–40	9–23	5–20	0.15	0.20
Ester (I) ¹²	15					

mortality counts taken after 24 and 48 hr.; each compound was tested in at least four concentrations and in quintuplicate. The results are listed in Table 1.

It is noteworthy that the toxicity of the compounds does not parallel the molecular weight. Both for mice and flies, the ethyl is much more toxic than either the methyl or the propyl compound. The sulphur compounds (IV) are much less toxic than the oxygen esters (I). It is further noteworthy that the most toxic substance does not necessarily reduce the amount of cholinesterase in blood or brain in the most pronounced manner. This is a further indication that the toxicity of the compounds is not, or at least not wholly, based on their anticholinesterase activity.

EXPERIMENTAL

Preparation of Dialkyl Phosphorothioites (II).—*Method 1.* Diethyl phosphorochloridite (72 g.), pyridine (37 g.), and light petroleum (450 ml.) were introduced into a nitrogen-filled flask. Hydrogen sulphide was then passed through the stirred mixture so that the gas was absorbed completely. When the exothermic reaction subsided and the gas was no longer absorbed, the pyridinium chloride formed was filtered off, and the filtrate distilled; diethyl phosphorothioite had b. p. 86.9°/26 mm. (yield, 81%).

Method 2. Phosphorus trisulphide (1 mol.) was refluxed with the alcohol (10 mol.) for varying periods: *viz.*, methanol, 20; ethanol, 12–15; propanol, 10; butanol, 9 hr. The product was isolated by distillation, yields being about 20%.

TABLE 2. *Dialkyl phosphorothioites (II).*

R	Method	B. p./mm.	Yield (%)	n_D	S (%)	
					found	calc.
Me	2	69–70°/30	20	1.4748 (27.0°)	25.1	25.1
Et	1, 2	86.9°/26	81; 20	1.4631 (27.0°)	20.8	20.7
Pr ⁿ	1, 2	112°/30	73; 20	1.4543 (30.5°)	17.0	17.4
Pr ⁱ	1, 2	95°/26	34; 20	1.4492 (39.0°)	17.6	17.4
Bu ⁿ	1, 2	148°/32	83; 20	1.4510 (30.5°)	15.2	15.1

The dialkyl phosphorothioites are colourless oils, which can be treated with water without causing dissolution or decomposition. In this way, dialkyl phosphites, which might contaminate the products, can be eliminated easily. These products are reported in Table 2.

⁹ Sheppard, *Trans. Faraday Soc.*, 1950, **46**, 429.

¹⁰ See Edery and Schatzberg-Porath, *Science*, 1958, **128**, 1137.

¹¹ Tahori, *J. Econ. Entomol.*, 1955, **48**, 638.

¹² van Asperen, *Ent. Expt. and Appl.*, 1958, **1**, 130.

OO-Dialkyl S-(2,2-Dichlorovinyl) Phosphorothioates (IV).—Diethyl phosphorothioite (0.9 mole) was added to chloral (1 mole), at 60°. The exothermic reaction was accompanied by a transient violet-red colour; the temperature of the mixture was kept below 80°. The yellowish product

TABLE 3. OO-Dialkyl S-(2,2-dichlorovinyl) phosphorothioates (IV).

R	B. p./mm.	Yield (%)	n		d		MR, fd.	[R _L] _D ¹³		Cl (%)		S (%)	
								calc. (IV)	calc. (IVa)	calc.	found	calc.	found
Me	113—115°/2	70	1.5235 (23.5°)	1.4442 (22.0°)	50.30	49.93	48.78	30.0	29.7	13.5	13.7		
Et	130°/5	70	1.5020 (25.0°)	1.3119 (22.0°)	59.60	59.76	58.00	26.8	26.5	12.1	12.4		
Pr ⁿ	135°/2	30	1.4870 (25.0°)	1.2350 (23.0°)	68.35	68.40	67.24	24.2	24.1	10.9	11.1		

was evacuated and distilled *in vacuo*, in the presence of a small quantity of quinol; the diethyl product had b. p. 130°/5 mm. (yield 70%). Other esters were obtained similarly and the properties are summarized in Table 3.

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¹³ For doubly bound phosphorus and sulphur, the atomic refractions 9.70 and 4.27 were used; for doubly bound oxygen the value characteristic for carbonyl-oxygen (2.21).