44. *Organic Phosphorus Compounds. Part I. The Reaction of Dialkyl Methylphosphonates and Methylphosphonothionates with Inorganic Acid Chlorides.*

By Zvi Pelchowicz.

Dialkyl methylphosphonates are converted by thionyl chloride or, better, oxalyl chloride into alkyl methylphosphonochloridates. These ester chlorides are formed, under the same conditions, from the dialkyl methylphosphonothionates, sulphur being formed as by-product. The mechanism of the latter reaction is discussed.

It has been observed[1] that reaction of phosphorus pentachloride with dialkyl methylphosphonates (I) gives methylphosphonyl dichloride in two steps, the time required for complete reaction increasing with increasing molecular weight of the alkyl group:

$$\mathrm{Me{\cdot}PO(OR)_2\ (I) + PCl_5 \longrightarrow Me{\cdot}POCl{\cdot}OR\ (II) + POCl_3 + RCl}$$

$$\mathrm{Me{\cdot}POCl{\cdot}OR + PCl_5 \longrightarrow Me{\cdot}POCl_2 + POCl_3 + RCl}$$

We have tried to use the differential reactivity of the two alkoxy-groups for the preparation of the synthetically valuable chlorides[2] (II). Hydrolysis with concentrated hydrochloric acid smoothly gave viscous products which were converted by thionyl chloride into the chlorides (II) in ~50% yield. From the infrared spectrum, it was concluded that the acidic viscous products are alkyl hydrogen methylphosphonates.[1a]

When the esters (I) were treated with boiling thionyl chloride, 80% yields of the chlorides (II) were obtained. The methyl and the isopropyl compound gave only polymers under these conditions, but use of oxalyl chloride gave good yields in all cases (Table 1). The analogous reaction with carbonyl chloride has been described.[3]

The parallel reaction of thionyl chloride with dialkyl methylphosphonothionates

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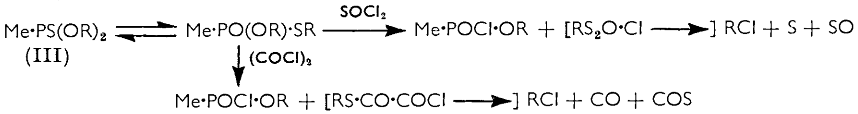
[1] Pelchowicz, unpublished work.

[1a] Cf. Rabinowitz, *J. Amer. Chem. Soc.*, 1960, **82**, 4564.

[2] Cf. Hudson and Kealy, *J.*, 1956, 2463; Coe, Perry, and Brown, *J.*, 1957, 3604; Razumov, Mukhacheva, and Markovich, *Zhur. obshchei Khim.*, 1957, **27**, 2389; Hoffmann, Simmons, and Glunz, *J. Amer. Chem. Soc.*, 1957, **79**, 3570; de Roos, *Rec. Trav. chim.*, 1959, **78**, 145.

[3] Coe, Perry, and Brown, see ref. 2; Coe, Perry, and Sherlock, *J. Org. Chem.*, 1959, **24**, 1018.

Me·PS(OR)_2, best prepared[4] by the interaction of methylphosphonothionyl dichloride Me·PSCl_2 with the sodium alkoxide in an excess of the alcohol, gave, not the expected ester chlorides of the thio-acid, but free sulphur and the ester chlorides (II). Analogous results were obtained with oxalyl chloride (Table 1); they may be explained by assuming that the starting compounds (III) are in equilibrium with the phosphonothiolates that are attacked as follows:



$$\underset{\text{(III)}}{\text{Me·PS(OR)}_2} \rightleftharpoons \text{Me·PO(OR)·SR} \xrightarrow{\text{SOCl}_2} \text{Me·POCl·OR} + [\text{RS}_2\text{O·Cl} \longrightarrow]\ \text{RCl} + \text{S} + \text{SO}$$

$$\text{Me·PO(OR)·SR} \xrightarrow{(\text{COCl})_2} \text{Me·POCl·OR} + [\text{RS·CO·COCl} \longrightarrow]\ \text{RCl} + \text{CO} + \text{COS}$$

(Sulphur monoxide, SO, has been observed as an unstable intermediate in many reactions.[5]) It is reasonable that the more basic sulphur atom is attacked more quickly than oxygen. It may be pointed out that the infrared spectrum of dimethyl methylphosphonothionate does not show the frequency typical for the P=O bond (1270 cm.$^{-1}$),[6] but has a strong band in the 750 cm.$^{-1}$ region, in which the P=S frequency is known to lie.[7]

The above hypothesis is supported by the behaviour of dimethyl methylphosphonothionate towards phosphorus pentachloride. In this case, both the thiono- and the thiolo-form reacted, and the following reactions took place:

$$\text{Me·PO(OMe)·SMe} + 2\text{PCl}_5 \longrightarrow \text{Me·POCl}_2 + \text{POCl}_3 + 2\text{MeCl} + \text{PCl}_3 + \text{S}$$

$$\text{Me·PS(OMe)}_2 + 2\text{PCl}_5 \longrightarrow \text{Me·PSCl}_2 + 2\text{POCl}_3 + 2\text{MeCl}$$

It has been pointed out above that phosphorus pentachloride is capable of reacting with both ester groups of a phosphonate.

The toxicity (for rats) of some of the compounds (II) was determined. For the ethyl compound LD$_{50}$ was 14 mg./kg., and for the isopropyl homologue 4·5 mg./kg. The higher toxicity of the secondary alkyl derivatives has been observed in similar cases.[8]

EXPERIMENTAL

Acid Hydrolysis of Diethyl Methylphosphonate.—This ester[9] (152 g., 1 mole) was mixed at room temperature with concentrated hydrochloric acid (300 ml.); a slightly exothermic reaction set in immediately; after refluxing for 1 hr., the excess of acid and water were removed *in vacuo*. The viscous residue was considered to be ethyl hydrogen methylphosphonate on the strength of its strongly acid reaction and the infrared bands (liquid film) at 3400, 3000 (Me), 1320 P–Me), 1230 (broad, P=O), 1030, 970, 900, 820, 780, and 720 cm.$^{-1}$.

For identification, it was treated in benzene (200 ml.) with thionyl chloride (113 g., 1 mole) in benzene (80 ml.) for 3 hr. The *ethyl methylphosphonochloridate* produced (yield, 62·5 g., 44%) distilled at 83—84°/23 mm. and had n_D^{25} 1·4320 (Found: Cl, 25·0. $\text{C}_3\text{H}_8\text{ClO}_2\text{P}$ requires Cl, 24·9%).

Reaction of Dialkyl Methylphosphonates with Thionyl Chloride.—A mixture of the dialkyl methylphosphonate (1 mole), in an equal volume of benzene, with thionyl chloride (2·5 moles) was refluxed for 3 hr., and then distilled *in vacuo*. The methyl and the isopropyl compound gave only polymers, but the following positive results were obtained: ethyl ester chloride, b. p. 83—84°/23 mm., n_D^{25} 1·4320 (yield, 80%); propyl ester chloride, b. p. 63°/4 mm., n_D^{19} 1·4378 (yield, 85%); n-butyl ester chloride, b. p. 70°/3 mm., n_D^{17} 1·4389 (yield, 87%).

Reaction of Dialkyl Methylphosphonates with Oxalyl Chloride.—To the dialkyl methylphosphonate (0·1 mole) in dry ether (150 ml.), oxalyl chloride (23·5 g., 0·115 mole), in ether (10 ml.),

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[4] Kabachnik and Godovnikov, *Doklady, Akad. Nauk S.S.S.R.*, 1956, **110**, 217; Razumov, Mukhacheva, Zaikonnikova, Godovnikov, and Rizpolozhenzkii, *Khim. i Primenenie fosfororg, Soedin. Akad. Nauk S.S.S.R.*, *Trudy* 1-*oi Conferents*, 1955, 205 (*Chem. Abs.*, 1958, **52**, 293); Hoffmann, Wadsworth, and Weiss, *J. Amer. Chem. Soc.*, 1958, **80**, 3945.

[5] See, *e.g.*, Schenk, *Z. anorg. Chem.*, 1933, **211**, 150; 1934, **220**, 268; 1936, **229**, 305; Woehler and Wegwitz, *ibid.*, 1933, **213**, 129.

[6] Corbridge, *J. Appl. Chem.*, 1956, **6**, 456.

[7] Pelchowicz, following paper; Hooge and Christen, *Rev. Trav. chim.*, 1958, **77**, 911; Gore, *Discuss. Faraday Soc.*, 1950, **9**, 138; Corbridge, ref. 6; Scott, Menefee, and Alford, *J. Org. Chem.*, 1957, **22**, 789, 792. Popov, Mastryukova, Rodionov, and Kabachnik, *Zhur. obshchei Khim.*, 1959, **29**, 1998.

[8] *E.g.*, Saunders and Stacey, *J.*, 1948, 695.

[9] *Org. Synth.*, 1951, **31**, 33.

was added at 0° with stirring. The mixture was kept at room temperature for 24 hr., then evaporated to remove the solvent and the alkyl chloride formed, and distilled *in vacuo*. The results are summarized in Table 1.

TABLE 1. *Alkyl methylphosphonochloridates* (II).

R	B. p./ mm.	n_D	d_4	$[R_L]_D$ calc.	$[R_L]_D$ found	Cl (%) calc.	Cl (%) found	Yield (%) (I) + $(COCl)_2$	Yield (%) (III) + $SOCl_2$	Yield (%) (III) + $(COCl)_2$
Me	73°/22	1·4395 (18°)	1·3005 (16°)	25·52	26·00	27·7	27·6	85	50	85
Et	83°/21	1·4385 (18°)	1·2095 (16°)	30·14	30·97	24·9	24·8	88	72	87
Pr^n	94°/21	1·4378 (18°)	1·1602 (16°)	34·76	35·41	22·7	22·7	87	80	95
Pr^i	83°/22	1·4285 (23°)	1·1479 (21°)	34·76	35·50	22·7	22·8	61	62	75
Bu^n	105°/19; 70°/3	1·4388 (15°)	1·1225 (16°)	39·38	39·77	20·8	20·9	93	82	91

Methylphosphonothionyl dichloride was prepared as follows[3]: Methylphosphonyl dichloride[10] (133 g., 1 mole) was refluxed with phosphorus pentasulphide (36 g., 0·25 mole) for 3—4 hr., until a dark homogeneous mass was formed. The product was distilled *in vacuo*, and the distillate washed three times with water (200 ml.), dried (Na_2SO_4), and fractionated; the product (124 g., 83%) had b. p. 154°/760 mm., 44—45°/9 mm., m. p. −25·8°, n_D^{25} 1·5485, d_4^{25} 1·4178, $[R_L]_D$ 33·43.

The dialkyl methylphosphonothionates were prepared according to directions of Hoffmann;[4] it was advantageous to wash the esters with water before distillation. Their constants were practically identical with those recorded in the literature. The molecular refractivities are summarized in Table 2.

TABLE 2. *Molecular refractivity of* $Me{\cdot}PS(OR)_2$.[11]

R	n_D	d_4^{25}	$[R_L]_D$ calc.	$[R_L]_D$ found	R	n_D	d_4^{25}	$[R_L]_D$ calc.	$[R_L]_D$ found
Me ...	1·4738 (25°)	1·1375	34·40	34·57	Pr^i ...	1·4570 (20°)	0·9889	52·88	53·83
Et ...	1·4630 (22°)	1·0510	43·64	43·94	Bu^n ...	1·4642 (17·5°)	0·9820	62·11	62·70
Pr^n ...	1·4640 (18°)	1·0097	52·88	53·46					

Reactions of Dialkyl Methylphosphonothionates.—(i) *With thionyl chloride.* To thionyl chloride (2·5 moles), the ester (1 mole) was added at room temperature. The spontaneous reaction, which was accompanied by precipitation of sulphur, was completed by refluxing the mixture for 2 hr. The sulphur was filtered off, and the alkyl methylphosphonochloridate fractionated (see Table 1).

(ii) *With oxalyl chloride.* To a solution of the ester (1 mole) in ether (200 ml.), oxalyl chloride (1·5 moles for the methyl ester, 1·75 moles for the ethyl and the isopropyl ester, 2 moles for the propyl and the butyl ester) in ether (200 ml.) was added at room temperature. After 24 hr. at room temperature, the ether and the excess of oxalyl chloride were distilled off, and the product was fractionated *in vacuo* (see Table 1).

Reaction of Dimethyl Methylphosphonothionate with Phosphorus Pentachloride.—In a 2-l. flask, chlorine was passed through a solution of phosphorus trichloride (275 g., 2 moles) in carbon tetrachloride (350 ml.). When all the trichloride had been converted into the pentachloride, the mixture was refluxed for 1 hr., and dimethyl methylphosphonothionate (142 g., 1 mole) added with cooling and stirring. A lively reaction took place, accompanied by dissolution of the phosphorus pentachloride and appearance of a yellow colour. The mixture was refluxed for 2 hr. and distilled quickly, in the later stages *in vacuo*. The residue consisted of sulphur, and also from the deep yellow distillate sulphur crystallised. Fractional distillation yielded: (1) carbon tetrachloride, containing 96·2 g. (0·7 mole) of phosphorus trichloride; (2) phosphorus oxychloride, 184 g. (1·2 moles); (3) b. p. 122—125°, 10 ml. (14·2 g.), a mixture of phosphorus oxychloride and $PSCl_3$; (4) b. p. 154° (13·3 g.), a mixture of $CH_3{\cdot}POCl_2$ and $CH_3{\cdot}PSCl_2$; by washing with cold water, the former was destroyed, whilst the latter (7·5 g.) remained unattacked (b. p. 154°, n_D^{25} 1·5485. Found: S, 21·50. Calc. for CH_3Cl_2PS: S, 21·47%), (5) b. p. 163—165° (86·5 g., 65%), methylphosphonyl dichloride.

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[10] Kinnear and Perren, *J.*, 1952, 3437.

[11] As atomic refractions for doubly bound sulphur and phosphorus, the values 9·70 and 4·27, respectively, were used.