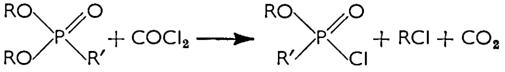
185. *The Mechanism of the Reaction between Carbonyl Chloride and Esters of Quinquevalent Phosphorus.**

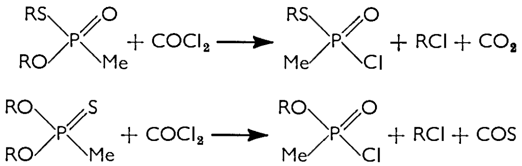
By M. Green and R. F. Hudson.

The reaction between several esters of quinquevalent phosphorus and carbonyl chloride are reported. Acetyl chloride reacts very slowly under the same conditions. By using benzyl methylphenyl[^{18}O]phosphinate, it is shown that the reaction involves the phosphoryl-oxygen atom exclusively within the limits of experimental error. The detailed reaction mechanism is discussed in the light of these results.

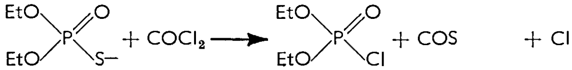
Several chlorinating agents (*e.g.*, thionyl chloride and phosphorus pentachloride) readily convert phosphorus esters into the corresponding chlorides, and in particular carbonyl chloride [1] removes one ester group only in a clean reaction to give the phosphonochloridate from the corresponding phosphonate. The products have been investigated for the methyl and isopropyl esters and high yields of the corresponding alkyl halides isolated. The reaction therefore proceeds as follows, without the formation of the corresponding chloroformate:



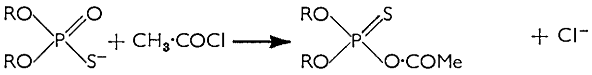
Cadogan [2] recently studied the behaviour of the analogous thioesters and showed that the thionate gives carbonyl sulphide, but the corresponding thiolate gives carbon dioxide:



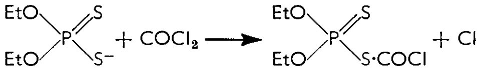
Moreover, the sulphur atom is removed in preference to the oxygen atom [2] by the reaction of the corresponding thiolic acid (in the form of the sodium salt):



This is surprising in view of the greater reactivity of the oxygen atom of thiolic acids towards acetyl chloride: [3]



The reaction between carbonyl chloride and the anion of a dithionic acid gives an intermediate anhydride which is readily isolated:



---

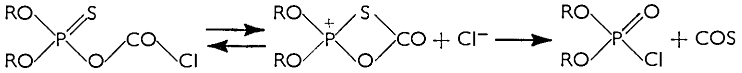
* Cf. *Proc. Chem. Soc.*, 1962, 217.

[1] Coe, Perry, and Brown, *J.*, 1957, 3604.

[2] Cadogan, *J.*, 1961, 3067.

[3] Kabachnik, Mastryukova, Rodionova, and Popov, *Zhur. obshchei Khim.*, 1956, **26**, 120.

Aaron *et al.*[4] have suggested that the corresponding anhydride, formed from the monothionic acid, can re-arrange as follows:



Cadogan [2] also made the important observation that the triesters, $(EtO)_3PO$, $(EtO)_3PS$, and $(EtO)_2\cdot(EtS)PO$ are not reactive under conditions comparable with those used in the reactions described above. We also find that, whereas dimethyl methylphosphonate is very reactive, methyl 1-naphthyl methylphosphonate is inert. Moreover, phosphinate esters are very reactive, giving essentially quantitative yields of the phosphinyl chloride very rapidly.

The reactivity order $RR'PO\cdot OMe > RO\cdot PR'O\cdot OMe > (RO)_2PO\cdot OMe$ which follows the increase in vibration frequency[5] of the P=O group, and the other observations described above, suggest that the phosphoryl-oxygen atom is the more nucleophilic centre.

This atom is known to be nucleophilic since phosphine oxides react readily with phosphorus pentachloride to give phosphoryl chloride.[6] Moreover, the phosphoryl group is involved in hydrogen bonding in preference to the alkoxyl group,[7] and Laughlin has suggested that the former is the more nucleophilic centre.[8] Cadogan has proposed a mechanism for the reaction with carbonyl chloride involving preliminary attack by the phosphoryl-oxygen atom.[2]

In order to obtain direct information on the position of bond fission we have studied the reaction between carbonyl chloride and an $[^{18}O]$phosphinate.

Benzyl $[^{18}O]$alcohol was prepared by the following route: [9]

$$Ph_2CCl_2 + H_2{}^{18}O \longrightarrow Ph_2C{=}^{18}O \xrightarrow{Ph\cdot CO_3H} Ph\cdot C^{18}O\cdot OPh \xrightarrow{LiAlH_4} Ph\cdot CH_2\cdot{}^{18}OH$$

and converted into the ester by reaction with methylphenylphosphinyl chloride. After reaction with a saturated solution of carbonyl chloride in carbon tetrachloride, the phosphinyl chloride was separated and converted into the phosphinic acid. The absence of exchange with ^{18}O in this type of reaction is well established[10] and is further confirmed by the present result. Reaction with di-*p*-tolylcarbodi-imide gives the corresponding urea:

$$PhMePO\cdot O\cdot CH_2Ph \xrightarrow{COCl_2} PhMePOCl \xrightarrow{H_2O} PhMePO\cdot OH \longrightarrow CO(NHPh)_2 + (PhMePO)_2O$$

Pyrolysis of this urea at 350° in the presence of activated bronze powder[10] gave carbon dioxide quantitatively.

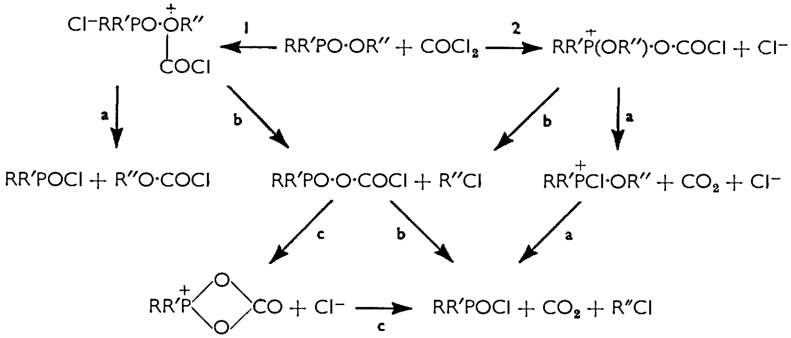
Starting from water containing 1·7 atoms % of ^{18}O, carbon dioxide containing 0·83(3) (±0·02) atom % of ^{18}O was obtained.

Since one-half of the isotope is lost in the reaction of the phosphinic acid with the carbodi-imide, it follows that, within the limits of experimental error, the phosphinyl chloride is produced without a change in the isotopic content. The oxygen atom of the phosphoryl group is consequently the nucleophilic centre.

The reaction mechanism, for which the alternatives formulated can be proposed, can now be considered. Mechanism 1a can be neglected, since the chloroformate which would be stable under the experimental conditions, was not isolated. Similarly, the reaction (c) leading to the cyclic intermediate[4] can be discounted, as in this case the ^{18}O content of the carbon dioxide would be half of that actually observed.

---

[4] Aaron, Uyeda, Frack, and Miller, *J. Amer. Chem. Soc.*, 1962, **84**, 617.
[5] Bell, Heisler, Tannenbaum, and Goldenson, *J. Amer. Chem. Soc.*, 1954, **76**, 5185.
[6] Kosolapoff, " Organic Phosphorus Compounds," Wiley, New York, 1958, p. 59.
[7] Aksnes, *Acta Chem. Scand.*, 1960, **14**, 1475.
[8] Laughlin, *J. Org. Chem.*, 1962, **27**, 1005; Harwood and Grisley, *J. Amer. Chem. Soc.*, 1960, **82**, 423.
[9] Doering and Dorfman, *J. Amer. Chem. Soc.*, 1953, **75**, 5595.
[10] Halmann, *J.*, 1959, 305.



It is not possible to make a definite decision between mechanisms 2a and 2b. We consider, however, that 2a is the more probable, since acetyl chloride in carbon tetrachloride does not react at room temperature in 24 hours. Since acetyl chloride and carbonyl chloride have comparable reactivities towards water and alcohols in dilute solution in dioxan,[11] these two chlorides should have similar reactivities towards the phosphinate in reactions of type 2b. By mechanism 2a, acetyl chloride would react to give an unfavourable equilibrium ($k_2 \gg k_1$):

$$\mathrm{RR'\overset{+}{P}(OR)\cdot OAc + Cl^-} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{RR'\overset{+}{P}Cl\cdot OR + AcO^-}$$

whereas carbonyl chloride would give the chloroformate ion which would rapidly decompose. It is interesting that acetyl fluoride does give the corresponding fluoridate and acetate,[12] and not the alkyl fluoride, as follows: $\mathrm{R'\cdot PO(OR)_2 + AcF \longrightarrow R'\cdot PFO\cdot OR + ROAc}$. This can be understood in view of the very high nucleophilic reactivity of the fluoride ion [13] towards the phosphorus atom.

A slow reaction was observed when acetyl chloride and the phosphinate ester were boiled for 24 hours in the absence of a solvent. High yields of benzyl chloride and the corresponding pyrophosphate were eventually obtained, probably by the following mechanism [cf. 2(b)]:

$$\mathrm{PhMePO\cdot O\cdot CH_2Ph + AcCl \longrightarrow PhMePO\cdot OAc + Ph\cdot CH_2Cl}$$

$$\mathrm{PhMePO\cdot OAc + PhMePO\cdot O\cdot CH_2Ph \longrightarrow (PhMePO)_2O + Ph\cdot CH_2\cdot OAc}$$

$$\mathrm{CH_2Ph\cdot OAc + AcCl \longrightarrow Ac_2O + Ph\cdot CH_2Cl}$$

The final stage of the reaction 2b, which involves the removal of an alkyl group from the quasi-phosphonium intermediate, is similar to the last stage of the Arbusov reaction. We find that di-(*L*-1-methylheptyl) methylphosphonate gives the *D*-chloride stereospecifically, showing that this stage proceeds with inversion of configuration, in agreement with a bimolecular reaction between a chloride ion and the intermediate. Inversion is similarly observed in the reaction with phosphorus pentachloride.

EXPERIMENTAL

Methyl methylphenylphosphinate was prepared by the known method [13] in 44% yield from dichlorophenylphosphine and had b. p. 104—106°/0·6 mm., n_D^{24} 1·5265 (Found: C, 56·2; H, 6·6. Calc. for $C_8H_{11}O_2P$: C, 56·5; H, 6·5%).

Methylphenylphosphinyl Chloride.—Methyl methylphenylphosphinate (28·5 g.) in carbon tetrachloride (50 ml.) was added dropwise (0·5 hr.), with ice-cooling and stirring, to a saturated solution of carbonyl chloride in carbon tetrachloride (100 ml.) through which a rapid stream

---

[11] Böhme, *Ber.*, 1941, **74**, 248.

[12] Yakobovich, Ginsburg, and Makarov, *Zhur. obshchei Khim.*, 1961, **31**, 1517.

[13] Dostrovsky and Halmann, *J.*, 1953, 508.

of carbonyl chloride was being passed. Then the mixture was left at room temperature overnight. The excess of carbonyl chloride and carbon tetrachloride was removed, and the residue was distilled. The product had b. p. 98°/0·5 mm., n_D^{20} 1·5595 (79%) (Found: C, 48·0; H, 4·7; Cl, 20·1. Calc. for C_7H_8ClOP: C, 47·9; H, 4·6; Cl, 20·2%).

Benzyl Methylphenylphosphinate.—Methylphenylphosphinyl chloride (2·5 g.) in dry ether (10 ml.) was added dropwise, with ice-cooling and stirring, to benzyl alcohol (1·35 g.) and triethylamine (1·26 g.) in dry ether (25 ml.). The mixture was left at room temperature overnight, washed with aqueous phosphate buffer (pH 7·0), dried ($MgSO_4$), and evaporated, and the residue was distilled. The *product* had b. p. 152—154°/0·5 mm. (67%) (Found: C, 68·0; H, 6·2; P, 12·9. $C_{14}H_{15}O_2P$ requires C, 68·3; H, 6·1; P, 12·6%).

(+)-1-*Methylheptyl Methylphenylphosphinate.*—The procedure was used as for the benzyl ester. Methylphenylphosphinyl chloride (17·4 g.) in ether (50 ml.) was added to (−)-octan-2-ol (13·0 g.), $[\alpha]_D^{22}$ −7·6° (homogeneous), and triethylamine (10·1 g.) in dry ether (100 ml.). The *product* (75%) had b. p. 113°/0·6 mm., n_D^{20} 1·4945, $[\alpha]_D^{22}$ +4·46° (homogeneous) (Found: C, 67·1; H, 9·6. $C_{15}H_{25}O_2P$ requires C, 67·2; H, 9·3%).

Reaction of Benzyl Methylphenylphosphinate with Carbonyl Chloride.—The procedure used was as for the preparation of methylphenylphosphinyl chloride. Benzyl methylphenylphosphinate (3·0 g.) in carbon tetrachloride (8 ml.) was added to a saturated solution of carbonyl chloride in carbon tetrachloride (25 ml.). Distillation yielded benzyl chloride (b. p 63°/8 mm.) and methylphenylphosphinyl chloride (1·4 g.), b. p. 90—92°/0·3 mm. The identity of both products was confirmed by their infrared spectra.

Reaction of Benzyl Methylphenylphosphinate with Acetyl Chloride.—(*a*) To the ester (5 g.) in carbon tetrachloride (50 ml.) was added acetyl chloride (12 g.). The solution was left at room temperature for 24 hr. No reaction occurred.

(*b*) The ester (5 g.) was boiled in acetyl chloride (50 ml.) for 24 hr. Distillation yielded benzyl chloride (2·2 g.) and a high-boiling material, b. p. 180°/0·05 mm. (2·6 g.), which on hydrolysis gave methylphenylphosphinic acid (2·75 g.).

Reaction of (+)-1-*Methylheptyl methylphenylphosphinate with Carbonyl Chloride.*—The same experimental procedure as above was used. The (+)-ester (15·0 g.) in carbon tetrachloride (50 ml.) was added to a saturated solution of carbonyl chloride in carbon tetrachloride (100 ml.). Distillation then yielded (+)-1-methylheptyl chloride (90%), b. p. 55—56°/10 mm., $[\alpha]_D^{22}$ +29·3° (homogeneous), n_D1·4269 (Found: Cl, 23·5. Calc. for $C_8H_{17}Cl$: Cl, 23·8%). Further distillation gave methylphenylphosphinyl chloride (72%), b. p. 100—104°/0·5 mm., having the correct infrared spectrum.

Reaction of Dimethyl Methylphosphonate with Carbonyl Chloride.—Dimethyl methylphosphonate (2 g.) in benzene (50 ml.) was treated with an excess of carbonyl chloride at 0°. The benzene was removed and the residue distilled, to give methyl methylphosphonochloridate (1·5 g.), b. p. 164—165°, n_D^{20} 1·4343.

Reaction of Di-isopropyl Methylphosphonate with Carbonyl Chloride.—Di-isopropyl methylphosphonate (10·0 g.) in benzene (250 ml.) was treated similarly with carbonyl chloride. Distillation gave isopropyl chloride (4·3 g.), b. p. 37°, and isopropyl methylphosphonochloridate (8·0 g.), b. p. 38—40°/1 mm.

Reactions of Methyl 1-*Naphthyl Methylphosphonate.*[14]—(*a*) *With carbonyl chloride.* The ester (1·0 g.) in benzene (25 ml.) was treated for 24 hr. with an excess of carbonyl chloride at 0°. The benzene was removed and the residue distilled, to give the starting material (0·95 g.), b. p. 125—130°/0·1 mm., n_D^{20} 1·5807.

(*b*) *With phosphorus pentachloride.* The ester (11·8 g.) in dry benzene (50 ml.) was boiled for 1 hr. with phosphorus pentachloride (8·6 g.). The benzene was removed and the residue distilled, to give 1-naphthyl methylphosphonochloridate, b. p. 144°/0·1 mm., m. p. 45—46° (lit., b. p. 144—145°/1 mm.; m. p. 46—47°).

Reaction of Di-(+)-1-*methylheptyl Methylphosphonate with Phosphorus Pentachloride.*—(*a*) Phosphorus pentachloride (2·5 g.) was boiled for 2 hr. with the ester (1·8 g.), prepared [15] from octan-2-ol ($[\alpha]_D^{20}$ +8·0°), in benzene (20 ml.). The benzene was removed, and the fraction of b. p. 58—60°/8—10 mm. was collected; it had n_D 1·4301 and $[\alpha]_D^{20}$ −19·5°.

(*b*) Phosphorus pentachloride (3·0 g.) was boiled for 1 hr. with di-(+)-1-methylheptyl methylphosphonate (3·6 g.) in dioxan. The mixture was poured into a saturated solution of

---

[14] Green and Hudson, *J.*, 1958, 3129.

[15] Gerrard, Green, and Nutkins, *J.*, 1952, 4076.

sodium hydrogen carbonate and extracted with ether. The extract was dried ($MgSO_4$) and distilled; the product had b. p. 70—71°/16 mm., n_D^{20} 1·4306, $[\alpha]_D^{20}$ −18·3°.

Benzyl [^{18}O]*Alcohol.*—Dichlorodiphenylmethane was treated with water containing 1·7 atoms % excess of oxygen-18, to give [^{18}O]benzophenone, m. p. 47—48°. This with perbenzoic acid yielded phenyl [*oxo*-^{18}O]benzoate, which was reduced by lithium aluminium hydride to benzyl [^{18}O]alcohol, b. p. 49°/1 mm., n_D^{20} 1·5400, having the correct infrared spectrum (cf. ref. 9).

Benzyl methylphenyl[^{18}O]phosphinate was prepared by the procedure described for the normal isotopic material.

Methylphenylphosphinyl chloride (1·3 g.) obtained by reaction of the [^{18}O] ester with carbonyl chloride was dissolved in water (10 ml.) and left overnight at room temperature. The water was then evaporated in a vacuum, giving methylphenylphosphinic acid (1·1 g.), m. p. 133—134°. This was dissolved in dry dioxan (20 ml.), and a solution of di-*p*-tolylcarbodi-imide (2·7 g.) in dry ether (10 ml.) (which had been centrifuged) was added. Di-*p*-tolylurea separated, and after 24 hr. was filtered off, washed with dry dioxan, and dried under reduced pressure. The material obtained had m. p. 268—269° (Found: C, 75·0; H, 6·5. Calc. for $C_{15}H_{16}N_2O$: C, 75·0; H, 6·7%). The di-*p*-tolylurea was heated in evacuated break-seal tubes with copper bronze (" triple deep gold bronze powder," Magna Manuf. Co. Inc., N.Y.), as described by Halmann.[10] The carbon dioxide formed was analysed mass-spectrometrically.

Analysis of the gas samples in the mass spectrometer identified carbon dioxide only. ~2·0 Ml. (N.T.P.) were obtained from 50 mg. of di-*p*-tolylurea, showing that a high conversion is achieved. Two samples gave (1) 0·833, (2) 0·833 (±0·02) atom % of ^{18}O in the carbon dioxide (initial ^{18}O content of the water, 1·70 atoms %).

We thank Dr. E. R. S. Winter of John and E. Sturge Ltd., Birmingham, for carrying out the ^{18}O analyses.

CYANAMID EUROPEAN RESEARCH INSTITUTE, 91 ROUTE DE LA CAPITE, COLOGNY-GENEVA,
SWITZERLAND.

[Present address (M. G.): DEPARTMENT OF CHEMISTRY, FACULTY OF TECHNOLOGY,
MANCHESTER UNIVERSITY, ENGLAND.]

[*Received, August 27th,* 1962.]