

## 27. *Experiments on the Interaction of Hydroxy-compounds and Phosphorus and Thionyl Halides in the Absence and in the Presence of Tertiary Bases. Part II.*

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Although the interaction of phosphorus oxychloride and (+) $\beta$ -octanol yielded evidence of the formation of the chlorophosphates,  $\text{POCl}_2\cdot\text{OR}$  and  $\text{POCl}(\text{OR})_2$ , it appears most probable that the pre-ionisation and internal decomposition of these are not responsible for the formation of any chloride,  $\text{RCl}$ , in the system. In the presence of pyridine, the behaviour of this alcohol is closely analogous to that of *n*-butyl alcohol (Gerrard, J., 1940, 1464).

Neither in the absence nor in the presence of pyridine was there any evidence of formation of chlorophosphates or phosphoric esters from (-)phenylmethylcarbinol; the chloride,  $\text{RCl}$ , was formed from the beginning of each operation.

Ethyl (-)mandelate, in the absence of pyridine, gave neither the chloride,  $\text{RCl}$ , nor chlorophosphates; but in the presence of pyridine, its behaviour may be described as intermediate between that of the other two hydroxy-compounds.

It is suggested that mechanisms comprising "end-on" and "broadside" oriented collisions appear in these systems; these are regarded as more probable than those involving the pre-ionisation of "intermediate" chloro-esters.

IN this experimental survey of the interaction of optically active  $\beta$ -octanol, phenylmethylcarbinol, or ethyl mandelate with phosphorus oxychloride in the absence and in the presence of pyridine, an attempt has been made to disentangle conditional and structural factors and to reveal possibilities of still further analyses by kinetic methods.

When (+) $\beta$ -octanol was mixed with the oxychloride at 15° there was no immediate evolution of hydrogen chloride, but a subsequent slow reaction evolved this gas and afforded a mixture of (-) $\beta$ -octyl chloride, the chlorophosphates  $\text{POCl}_2\cdot\text{OR}$  and  $\text{POCl}(\text{OR})_2$ , and the ester,  $\text{PO}(\text{OR})_3$ . It is believed that the chloride,  $\text{RCl}$ , was formed concurrently with the chlorophosphates, and not by a unimolecular decomposition or by subsequent ionisation of these. These chlorophosphates could not be isolated in a pure state, as was done with the *n*-butyl compounds (Gerrard, *loc. cit.*) and with the  $\beta$ -octyl chlorophosphites (Part I, J., 1944, 85), but the corresponding phosphoric esters were obtained by hydrolysis. The chlorophosphates were slowly formed by the interaction of the oxychloride and the ester  $\text{PO}(\text{OR})_3$ ; but no more than a trace of chloride,  $\text{RCl}$ , could be obtained by the specified treatment of these mixtures.

(-)Phenylmethylcarbinol and the oxychloride reacted slowly at 0° without the evolution of hydrogen chloride, and the products were (+) $\alpha$ -chloroethylbenzene and a residue which did not contain phosphoric esters (cf. Kenyon, Phillips, and Taylor, J., 1931, 382). There was not the slightest indication of the formation of chlorophosphates.

Ethyl (-)mandelate and the oxychloride interacted slowly, even at 60°, and produced neither the chloride,  $\text{RCl}$ , nor phosphoric esters; the highly viscous mass obtained as a residue was not further examined. Thionyl chloride (Part I, *loc. cit.*) gave rise to the chlorosulphinates, and phosphorus trichloride (*ibid.*) to the chlorophosphites.

The use of pyridine in the reaction with (+) $\beta$ -octanol had two functions. Addition of the oxychloride ( $\frac{1}{3}$  mol.) to the mixture of alcohol (1 mol.) and base (1 mol.) resulted in nearly theoretical yields of pyridine hydrochloride and the ester,  $\text{PO}(\text{OR})_3$ . Continued addition of the oxychloride then converted, under favourable conditions, the ester into a mixture of chlorophosphates, which did not yield the chloride,  $\text{RCl}$ , in the presence of the pyridine hydrochloride, although when free pyridine was present, the mixture gave the chloride,  $\text{RCl}$ , in strict analogy with the example of *n*-butyl alcohol (Gerrard, *loc. cit.*). Houssa and Phillips (J., 1932, 108),

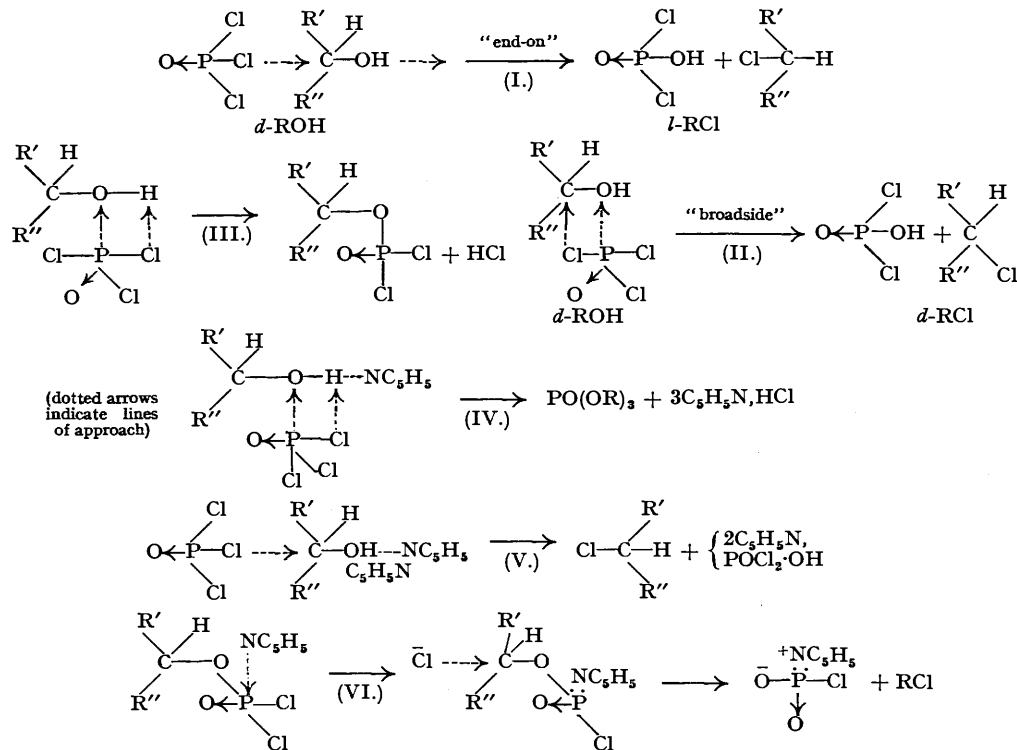
from the oxychloride (1 mol.),  $\beta$ -octanol (1 mol.), and pyridine (2 mols.) in ethereal solution, obtained ultimately only phosphoric esters.

The white solids precipitated when pyridine was added to the reaction mixture of alcohol and oxychloride, or of the tri-ester and oxychloride, were essentially phosphorus compounds, probably mixed with pyridine hydrochloride, and resulted from the interaction of pyridine with the products of reactions that had already occurred. Analytical results indicated the ratio  $2C_5H_5N : POCl_2 \cdot OH$ . The precipitate could not be due to unchanged oxychloride, because this compound and pyridine when mixed in dry ethereal solution formed only a trace of precipitate, and none at all in absence of ether.

(-)-Phenylmethylcarbinol gave no sign of phosphoric ester formation, even in presence of pyridine. Addition of oxychloride to the mixture of alcohol and base in ethereal solution at  $0^\circ$  caused production of (+)- $\alpha$ -chloroethylbenzene from the beginning, and the precipitate formed at the same time had a composition represented by  $2Cl, 2C_5H_5N, P$ , and probably  $2O$ . The rotatory power of the chloride,  $RCl$ , increased as the proportion of pyridine was increased.

Ethyl (-)-mandelate, when mixed with pyridine in ethereal solution and then treated with phosphorus oxychloride, yielded both ethyl (+)-phenylchloroacetate and phosphoric esters from the beginning of the reaction. Increase in the proportion of oxychloride increased the proportion of the chloroacetate with respect to the phosphoric ester, and in absence of ether, from (-)-mandelate (1 mol.), pyridine (1 mol.), and oxychloride (1 mol.) an excellent yield of (+)chloroacetate was produced. It is remarkable that for more than  $\frac{1}{3}$  mol. of the oxychloride, the analytical data for the precipitate are similar to those stated for the other two hydroxy-compounds. Wagner-Jauregg (*Helv. Chim. Acta*, 1929, 12, 61) showed that pyridine facilitated formation of the chloride,  $RCl$ , from methyl mandelate, 2 mols. of pyridine for 1 mol. of each of the other compounds being used. An interesting comparison is afforded by Fischer and Pfahler (*Ber.*, 1920, 53, 1606), who showed that even at  $-20^\circ$  phosphorus oxychloride and pyridine converted ethylene glycol into chloroethyl dihydrogen phosphate.

It is now suggested that the observations reported may be explained in terms of mechanisms involving oriented collisions either "end-on" (inversion) or "broadside" (retention), as in the accompanying scheme.



With (+)- $\beta$ -octanol in absence of ether, mechanisms (I) and (III) predominate, although (II) proceeds to some extent and reduces the rotatory power of the (-)-chloride,  $RCl$ , formed. In presence of pyridine (1 mol.), (IV) will proceed, and if sufficient oxychloride is used, the chlorophosphates will be formed from the tri-ester, and in the presence of free base mechanism (VI) (cf. Kenyon, Phillips, and co-workers) can then operate. Inversion without loss of rotatory power is to be expected from (IV) and (VI), and this is supported by experiment.

(-)-Phenylmethylcarbinol is converted into (+)-chloride,  $RCl$ , entirely by mechanisms (I) and (II), (I) predominating but (II) being quite large and giving rise to considerable loss of activity. In the presence of pyridine, there is a strong tendency for (V) to proceed exclusively; but if there is insufficient pyridine present,

some alcohol molecules will be denuded (2 molecules of pyridine are precipitated for each phosphorus atom) and will come under the influence of mechanisms (I) and (II). The production of (+)- $\alpha$ -chloroethylbenzene having a high rotatory power is therefore explained. When the (-)alcohol ( $\alpha_D^{20} - 18.4^\circ$ ) was added to the oxychloride stirred by a current of hydrogen chloride at  $0^\circ$ , an 80% yield of (-)- $\alpha$ -chloroethylbenzene ( $\alpha_D^{16} - 2.8^\circ$ ), predominating retention, was quickly formed. If it be assumed that an addition compound (VII) is formed, similar to that suggested by Levene and Rothen (*J. Biol. Chem.*, 1939, **127**, 237) for the action of hydrogen bromide (cf. Balfe and Kenyon, *Ann. Reports*, 1942, **39**, 120), then the presence of oxychloride and/or



the reaction product,  $\text{POCl}_2\text{-OH}$ , may facilitate removal of water and give the retention reaction an advantage. There is, however, another possibility depending on the facilitation of the broadside collision by the formation of a hydrogen bond,  $\text{ROH} \dots \text{O} \leftarrow \text{P} \text{Cl}_3$ . This is not unlikely, for Audrieth and Steinman (*J. Amer. Chem. Soc.*, 1941, **63**, 2115) have shown that, whereas the heat of mixing of the oxychloride and chloroform was 482 cal./g.-mol. probably indicative of hydrogen bond formation,  $\text{CCl}_3\text{H} \dots \text{O} \leftarrow \text{P} \text{Cl}_3$ , yet there was no heat effect when the oxychloride was mixed with carbon tetrachloride. Indeed, there appears to be no reason for excluding the influence of the hydrogen bond on mechanisms (I) and (II).

The author does not exclude the possibility of pre-ionisation, suggested by the work of Kenyon and Phillips (*Trans. Faraday Soc.*, 1930, **26**, 451; cf. Arcus, J., 1944, 236) and Hughes and Ingold (J., 1937, 1252) and their respective co-workers; but it is necessary to point out that Hughes and Ingold's experiments were conducted on the hydrolysis of halides,  $\text{RX}$ , under conditions very different from those existing in the systems now considered. Those experiments of Kenyon and Phillips which appear to be comparable with those of Hughes and Ingold were conducted in hot alcoholic solution and involved the interaction of toluene-*p*-sulphonic esters with alkali salts of either carboxylic acids or hydrogen halides.

In the view of Bateman, Hughes, and Ingold (J., 1944, 243) it is still not known whether, or in what circumstances, the formation of an organic chlorosulphinate,  $\text{R}\cdot\text{O}\cdot\text{SOCl}$ , is a single or a composite process. It might be formed by a bimolecular reaction between the molecule of thionyl chloride and a molecule of the hydroxy-compound, or by a slow pre-ionisation stage, followed by a rapid association of appropriate ions. Nevertheless, in the author's view (cf. Part I) there appears to be nothing against the mechanism involving the broadside collision similar to that depicted in (III).

The conclusion drawn by Boyd and Ladhams (J., 1928, 215) with the implication of generality, that the function of pyridine in facilitating phosphoric ester and chloride,  $\text{RCl}$ , formation is due to the reactivity of an addition compound,  $2\text{C}_5\text{H}_5\text{N}\cdot\text{POCl}_3$ , stands very precariously even on their own experiments with diaryloxyisopropyl alcohols. Considerable excesses of base and of oxychloride were used, and it was necessary to use chloroform as a solvent in order to obtain a complex which with water gave a 96% yield of the mono-phosphoric ester; but in a parallel experiment the same complex was assumed to be formed without the use of chloroform, and when the complex was heated, a 77% yield of the chloride  $\text{RCl}$  was obtained. Chloroform was deemed to be necessary because the effective concentration of the reactive addition compound, reduced by its insolubility in pyridine, was maintained by its solubility in chloroform. The insolubility of their addition compound in carbon tetrachloride would suggest the formation of  $\text{CCl}_3\text{H} \dots \text{NC}_5\text{H}_5$  and  $\text{CCl}_3\text{H} \dots \text{O} \leftarrow \text{P} \text{Cl}_3$  in chloroform, in accordance with the reference to the observation of Audrieth and Steinman (*loc. cit.*). Boyd and Ladham's claim of support by analogies is not established; McKenzie and Gow (J., 1933, 705), for example, believed that the retardation of the velocity of halogenation by thionyl chloride caused by the use of excess of pyridine was actually due to the formation of the addition compound  $(\text{C}_5\text{H}_5\text{N})_2\cdot\text{SOCl}_2$ .

Since ethyl mandelate gave neither the chloride,  $\text{RCl}$ , nor the chlorophosphates, it must be concluded that mechanisms (I), (II), and (III) do not operate. In the presence of pyridine, the mandelate resembles  $\beta$ -octanol in the formation of phosphoric ester, but also resembles phenylmethylcarbinol in that chloride,  $\text{RCl}$ , is formed from the outset, presumably by mechanism (V). It is in accordance with general principles that the effect of the phenyl group should be moderated by that of the carboxyl group.

The experiments now discussed have significance in biochemical phosphorylation, and may explain the low yields often found (*e.g.*, Gulland and Hobday, J., 1940, 746). In Plimmer and Burch's experiments (J., 1929, 279) formation of chloride,  $\text{RCl}$ , was not observed although the alcohols (cetyl and chloroethyl; cholesterol) were refluxed for several hours with the oxychloride in chloroform solution; after treatment with water, phosphoric esters were obtained. An attempt to prepare cetylphosphoryl chlorides by heating molecular proportions for 6 hours led to the isolation of cetene only. They could not repeat the experiment of Euler and Bernton (*Ber.*, 1927, **60**, 1721), who reported an unspecified yield of mono- and di-ester (no mention being made of chloride formation) from the action of the oxychloride on cholesterol in the presence of pyridine. Plimmer and Burch appeared to prefer the use of oxychloride alone.

The work now described has also an essential bearing on the interaction of hydroxy-compounds and phosphorus pentachloride; for if the primary reaction is  $\text{PCl}_5 + \text{ROH} \longrightarrow \text{RCl} + \text{POCl}_3 + \text{HCl}$ , the oxychloride may react on its own account and have a considerable influence on the nature and yields of products.

## EXPERIMENTAL.

**General Procedures.**—The hydroxy-compounds and the oxychloride reacted slowly at 0°, and mixing could be done quickly without appreciable evolution of heat. After the reaction mixture had been kept for the time and at the temperature stated, it was poured on ice and given "aqueous treatment," which comprised extraction of the oil with ether, washing the ethereal solution with a solution of sodium carbonate to extract acid and acid phosphoric esters, acidification (dilute sulphuric acid) of the carbonate solution, and extraction with ether of any acid ester which separated. The two ethereal solutions were separately dried (sodium sulphate) and evaporated. Phosphate and chloride ions were quantitatively determined in the sum of the aqueous liquids in order to follow the fate of the respective elements.

When pyridine was used in ethereal solution, the oxychloride, also in ethereal solution, was added dropwise to an ethereal solution of the hydroxy-compound and base, and after a specified time the liquid was decanted from the white solid and poured on ice. The solid was washed with three small amounts of dry ether, placed in a vacuum for 2 hours, and analysed. The ethereal washings were added to the original ethereal solution and given the aqueous treatment already described. When the operation was conducted in absence of ether, the mixture of the precipitate and liquid was given aqueous treatment. Aqueous liquids were examined quantitatively for pyridine and chloride and phosphate ions. Rotatory powers are expressed for 1 dm.

**Interaction of (+)β-Octanol,  $\alpha_D^{18} + 8.0^\circ$ , and Phosphorus Oxychloride.**—Attempts to prepare pure specimens of the chlorophosphates  $\text{POCl}_2\cdot\text{OR}$  and  $\text{POCl}(\text{OR})_2$  by the method used for the corresponding *n*-butyl compounds and for the chlorophosphites of β-octanol (Part I, *loc. cit.*) were unsuccessful. In a series of trials, the primary product from the addition of alcohol (1 mol.) to oxychloride (2 mols.) was kept for different periods of time at 15°/15 mm., 30–40°/15 mm., or 15°/15 mm. in a desiccator containing solid sodium hydroxide, in the endeavour to remove excess of oxychloride; but octylene was formed and the chlorine content remained high (Found: Cl, 35.0, 35.8, 34.8%, for three different experiments). Very little chloride, RCl, could be obtained by distillation, either before or after aqueous treatment.

In the following series of experiments, (+)β-octanol (3.25 g., 1 mol.) was mixed at 0° with the stated amount of oxychloride.

(1) With oxychloride (0.33 mol.) after 30 mins.' standing at 15° there were obtained (–)β-octyl chloride (0.5 g.), b. p. 63–64°/16 mm.,  $\alpha_D^{18} - 23.1^\circ$ ,  $n_D^{20} 1.4256$ ; unchanged alcohol (1.0 g.); a residue (0.35 g.) (Found: P, 7.2%); and from the carbonate solution, a residue (1.3 g.),  $\alpha_D^{18} + 1.75^\circ$ ,  $n_D^{20} 1.4345$  (Found: P, 11.4%). The phosphoric esters could not be distilled and were not purified. The phosphorus contents of each of these specimens are recorded to indicate probable constitution and to show the fate of this element. The theoretical values for the tri-, di-, and mono-ester respectively are P, 7.1, 9.6, 14.8%.

(2) With oxychloride (0.5 mol.), after 24 hours at 15°, there were obtained (–)β-octyl chloride (1.3 g.), b. p. 57–59°/13 mm.,  $n_D^{18} 1.4269$ ,  $\alpha_D^{18} - 23.8^\circ$ ; unchanged alcohol (0.9 g.); a residue (0.45 g.); and from the carbonate solution, a residue (0.4 g.) (Found: P, 12.3%).

(3) From oxychloride (1 mol.), and 1 hour's standing at 15°/15 mm., there resulted (–)β-octyl chloride (1.05 g.), b. p. 64–66°/17 mm.,  $\alpha_D^{18} - 20.1^\circ$ ,  $n_D^{18} 1.4276$ ; unchanged alcohol (0.6 g.); a residue (0.5 g.),  $n_D^{22} 1.4380$  (Found: P, 6.5%); and from the carbonate solution, a residue (1.15 g.),  $n_D^{18} 1.4368$  (Found: P, 13.4%) (compare Houssa and Phillips, *loc. cit.*). Distillation of the primary mixture before aqueous treatment did not increase the yield of chloride.

Slow addition of the oxychloride (3.3 g., 0.86 mol.) to the alcohol (3.3 g., 1 mol.) in a stream of carbon dioxide at 0°, followed by standing at 15° for 12 hours and then aqueous treatment, led to the isolation of (–)β-octyl chloride (1.6 g.), b. p. 64°/16 mm.,  $n_D^{18} 1.4262$ ,  $\alpha_D^{18} - 24.8^\circ$ , and a residue (1.3 g.),  $n_D^{18} 1.4400$ . The latter (Found: Cl, 10.0; P, 9.6%) was probably a mixture of the chlorophosphate,  $\text{POCl}(\text{OR})_2$  (Calc.: Cl, 10.4; P, 9.1%), and the di-ester,  $\text{PO}(\text{OR})_2\text{OH}$  (Calc.: P, 9.6%), aqueous treatment effecting only a slow hydrolysis of the chlorophosphate and slow extraction of the di-ester. The alkaline extract in the aqueous treatment gave a trace of oil on acidification.

**Interaction of (+)β-Octanol,  $\alpha_D^{18} + 8.0^\circ$ , and Phosphorus Oxychloride in Presence of Pyridine.**—With the reagents in ethereal solution at –10° the precipitation of pyridine hydrochloride commenced at the beginning of the dropwise addition of the oxychloride (2.6 g., 0.33 mol.) to the alcohol (6.5 g., 1 mol.) in the presence of pyridine (3.96 g., 1 mol.), and 25 minutes after the mixture had been removed from the cooling bath, 50% of the final amount of precipitate had formed. The rate of precipitation was therefore very much slower than with the trichloride (Part I). After 2 days at room temperature the ethereal solution was filtered from the precipitate (5.6 g.) (Found: Cl, 30.5. Calc.: Cl, 30.7%), and given aqueous treatment. Only a trace of chloride and phosphate ions was found in the wash-water. On evaporation of the ethereal solution, and keeping the residue for 1 hour at 40°/15 mm., (+)tri-β-octyl phosphate (6.59 g.),  $\alpha_D^{18} + 8.8^\circ$ ,  $n_D^{18} 1.4380$  (Found: P, 7.8.  $\text{C}_{24}\text{H}_{51}\text{O}_4\text{P}$  requires P, 7.1%), was obtained. This could not be further purified.

With the alcohol (3.25 g., 1 mol.) and the stated molecular proportions of the other reagents, mixed in absence of ether at –10°, the following experiments were conducted.

(1) With oxychloride (0.33 mol.) and pyridine (1 mol.) a semi-solid mass was formed. This was heated for 1 hour at 70–75°, and aqueous treatment then yielded a fair specimen of the tri-ester (2.8 g.),  $\alpha_D^{18} + 9.3^\circ$ ,  $n_D^{18} 1.4400$  (Found: P, 7.9%), and the carbonate solution gave no oil on acidification. The aqueous washings contained only a trace of phosphate ions.

(2) With exactly the same procedure, and with oxychloride (1 mol.) and pyridine (1 mol.), octylene (0.3 g.), a residue (1.65 g.),  $\alpha_D^{18} + 8.0^\circ$ ,  $n_D^{18} 1.4434$  (Found: P, 10.2%), and from the carbonate solution, a residue (1.7 g.),  $n_D^{18} 1.4379$  (Found: P, 13.1%), were obtained. Under these conditions pyridine was present as the hydrochloride and this did not facilitate decomposition of chlorophosphate to the chloride, RCl.

(3) With the same procedure, and with the oxychloride (1 mol.) and pyridine (2 mols.), (–)β-octyl chloride (1.2 g.), b. p. 69°/24 mm.,  $n_D^{18} 1.4305$ ,  $\alpha_D^{18} - 26.9^\circ$ , and a residue (1.6 g.),  $n_D^{18} 1.4438$ ,  $\alpha_D^{18} + 13.5^\circ$  (Found: P, 9.1%), were obtained; but no oil separated when the carbonate solution was acidified. The acid ester, extracted by carbonate solution in (2), was probably the hydrolytic product of the dichlorophosphate,  $\text{POCl}_2\cdot\text{OR}$ ; and it is this dichlorophosphate which in presence of free base in (3) yielded the chloride, RCl. When the primary mixture was kept at 80–90° for 1 hour, a greater yield of chloride (1.6 g.) and a smaller amount of residue (0.8 g.) were formed, presumably owing to conversion of some of the mono- into the di-chloride:  $\text{POCl}(\text{OR})_2 \rightarrow \text{POCl}_2\cdot\text{OR}$ .

(4) With the same proportions as in (2), but with 1 hour's reaction at 90–100°, the products were β-octyl chloride (0.5 g.), octylene (1.8 g.), and a residue (0.2 g.). The carbonate solution gave no oil on acidification, and the aqueous washings contained substantially all the phosphorus, and 94% of the chlorine in the system. In these circumstances, the dichloro-ester,  $\text{POCl}_2\cdot\text{OR}$ , yielded octylene and not chloride, RCl.

When more than 1 mol. of pyridine was used, the aqueous solutions contained alkylpyridinium ion and gave a yellow precipitate with an acidified solution of potassium ferrocyanide (Gerrard, J., 1936, 688; cf. also Boyd and Ladhams, *loc. cit.*).

Addition of the alcohol (4.3 g., 1 mol.) to the oxychloride (10.2 g., 2 mols.), followed by warming at 40°/15 mm. for 12 hours in the endeavour to remove excess oxychloride, led to formation of a residue (7.75 g. Calc. for dichlorophosphate: 8.2 g.) (Found: Cl, 35.8%), which with pyridine yielded a white solid (8.5 g.) and a supernatant liquid. The latter

together with the ethereal washings of the solid afforded, after aqueous treatment, octylene and ( $-$ ) $\beta$ -octyl chloride (0.55 g.), b. p. 59°/13 mm.,  $\alpha_D^{25}$  -27.9°. The solid was not a pure substance (Found: Cl, 23.2; P, 10.2;  $C_8H_{17}N$ , 53.5. Calc. for  $POCl_2 \cdot OH, 2C_8H_{17}N$ : Cl, 24.3; P, 10.6;  $C_8H_{17}N$ , 54.1%), and it was probably formed by interactions (i) of the base and dichlorophosphoric acid,  $POCl_2 \cdot OH$ , a reaction product, and (ii) of any dichlorophosphoric ester left undecomposed at the time of addition of base, the chloride  $RCl$  being the other product of this interaction.

The alcohol (2.65 g., 1 mol.) and oxychloride (2 mols.) were mixed and kept at 15°/13 mm. for 9 hours, and the product (Found: Cl, 34.8%) when treated with pyridine (2.0 g.) in ethereal solution gave a precipitate (4.38 g.) (Found: Cl, 21.7; P, 11.6;  $C_8H_{17}N$ , 42.9%).

The alcohol (2.6 g., 1 mol.) and oxychloride (3.07 g., 1 mol.) were mixed, and after 2 hours at 15° addition of pyridine (1.6 g., 2 mols.) afforded a precipitate (3.65 g.) (Found: Cl, 22.9; P, 10.3;  $C_8H_{17}N$ , 41.2%); from the ethereal extract octylene (0.9 g.), ( $-$ ) $\beta$ -octyl chloride (1.1 g.), b. p. 68°/23 mm.,  $\alpha_D^{18}$  -25.4°, and a residue (0.45 g.) were obtained. It is interesting to compare these precipitates with that obtained by the interaction of *n*-butoxyphosphoryl dichloride and pyridine (Gerrard, *loc. cit.*), which was partly separated into two solids having Cl, 18.8, 18.7; P, 14.8, 12.7;  $C_8H_{17}N$ , 41.6, 38.0%, respectively.

**Effect of Mixing Phosphorus Oxychloride and Pyridine.**—Since Boyd and Ladhams (*loc. cit.*) attributed the function of pyridine in their experiments on aryloxyisopropyl alcohols to the formation of a reactive addition compound,  $POCl_2 \cdot 2C_8H_{17}N$ , which, they state, is formed as a crystalline solid when the reagents are mixed in ethereal solution, it was necessary to consider in this light the precipitates described in the foregoing. Boyd and Ladhams mixed pyridine (12 g.) and oxychloride (10 g.) in ethereal solution and immediately obtained an oil which soon solidified (7.4 g.) (Found: Cl, 27.8; P, 9.2. Calc. for  $POCl_2 \cdot 2C_8H_{17}N$ : Cl, 34.1; P, 9.9%), but their analysis seems more in accordance with a mixture of the compound  $POCl_2 \cdot OH, 2C_8H_{17}N$  and pyridine hydrochloride, which could be due to the adventitious absorption of 1.6% of moisture by the reagents used. To test this hypothesis, three parallel experiments were conducted.

(1) The oxychloride (3.84 g., 1 mol.) was added quickly to pyridine (3.95 g., 2 mols.) in dry ether (40 c.c.) at 0°. A small amount of white solid (0.318 g.) (Found: Cl, 20.16; P, 6.0;  $C_8H_{17}N$ , 65.0%) separated at once, and no further change took place during 48 hrs. at 15°.

(2) With the same quantities, but with water (0.45 g.) added to the ethereal solution of pyridine, an oil which crystallised as described by Boyd and Ladhams was produced on the addition of the oxychloride. The ethereal solution was decanted, the solid rapidly washed with dry ether, and placed in a vacuum desiccator for 2 hours (4.42 g.) (Found: Cl, 22.6; P, 7.0;  $C_8H_{17}N$ , 53.2%).

(3) When atmospheric moisture was allowed to enter the reaction flask containing the dry reagents, by occasional removal of the stopper, the resulting solid had the composition Cl, 22.4; P, 9.8;  $C_8H_{17}N$ , 54.5 (Calc. for  $POCl_2 \cdot OH, 2C_8H_{17}N$ : Cl, 24.2; P, 10.6;  $C_8H_{17}N$ , 53.9%).

**Interaction of Tri- $\beta$ -octyl Phosphate and Phosphorus Oxychloride.**—The following experiments were conducted with specimens of the ester (4.34 g., 1 mol.) prepared as described in the foregoing.

(1) There was no heat effect when the oxychloride (6.0 g., 4 mols.) was added at 15°. After 48 hours at 15°, then 48 hours at 15 mm. in a desiccator containing solid sodium hydroxide, the product (6.4 g.) Calc. for dichlorophosphate,  $POCl_2 \cdot OR$ : 7.4 g.) (Found: Cl, readily hydrolysed, 22.3; P, 15.1. Calc. for  $POCl_2 \cdot OR$ : Cl, 28.7; P, 12.55%) was given aqueous treatment, and  $\beta$ -octyl chloride (0.4 g.), a residue (0.5 g.), and from the carbonate solution, a residue (1.3 g.) (Found: P, 13.1%), were obtained.

(2) With the oxychloride (2 mols.) and the mixture at 15° for 60 hours, aqueous treatment then yielded  $\beta$ -octyl chloride (0.48 g.), a residue (1.21 g.) (Found: P, 10.2%), and from the carbonate solution, a residue (1.32 g.) (Found: P, 14.2%). These results show the presence of the chlorophosphates in the reaction mixture.

(3) With the oxychloride (0.5 mols.), and the mixture at 15° for 48 hours at 15 mm. over solid sodium hydroxide for 24 hours, the product was *di- $\beta$ -octyloxyphosphoryl chloride* (5.1 g.) (Found: Cl, 10.7; P, 9.8.  $C_{16}H_{32}O_2Cl_2P$  requires Cl, 10.4; P, 9.2%); after aqueous treatment, this yielded no  $\beta$ -octyl chloride, but a residue (3.5 g.),  $n_D^{16}$  1.4432 (Found: P, 9.6%), and from the carbonate solution, a residue (0.5 g.),  $n_D^{15}$  1.4392 (Found: P, 12.1%). These results show that the primary product was essentially the monochlorophosphate and a little of the dichloro-ester.

The use of oxychloride (0.9 mol.), the mixture being kept at 15° for 60 hours, increased the proportion of the dichloro- at the expense of the monochloro-ester.

A mixture of the tri-ester (6.59 g. 1 mol.) and oxychloride (4.5 g., 1.5 mols.) was kept at 60° for 2.5 hours. 4 G. of this product, after aqueous treatment, yielded  $\beta$ -octyl chloride (0.3 g.) and a residue (1.0 g.) of phosphoric esters. 7.0 G. of the primary product were treated with pyridine (5 g.) at -10°. Precipitation of white solid was slow but became faster as the temperature rose to 15°. After 12 hours the colourless liquid was decanted, and the residue washed with dry ether, the washings being added to the decanted liquid for aqueous treatment. The solid weighed 4.00 g. (Found: Cl, 20.7;  $C_8H_{17}N$ , 48.0%). From the ethereal solution, ( $-$ ) $\beta$ -octyl chloride (1.55 g.), b. p. 68°/22 mm.,  $\alpha_D^{18}$  -21.1°, and a residue (1.72 g.),  $n_D^{15}$  1.4440,  $\alpha_D^{18}$  +14.1° (Found: P, 8.6%), were obtained, showing that both chlorophosphates were formed; but it was only the dichloro-ester which reacted with pyridine at room temperature.

When the tri-ester (2.8 g., 1 mol.) was kept for 2 days at 15° with only 0.5 mol. of the oxychloride and then heated with pyridine (1 mol.) for 1 hour at 100°, it yielded octylene (0.5 g.), ( $-$ ) $\beta$ -octyl chloride (1.3 g.), b. p. 68°/23 mm.,  $\alpha_D^{18}$  -9.2°, and a residue (0.3 g.). Apparently the monochloro-ester, too, interacted with pyridine at 100°, a behaviour resembling that of di-*n*-butoxyphosphoryl chloride (Gerrard, *loc. cit.*).

**Interaction of ( $-$ )Phenylmethylcarbinol and Phosphorus Oxychloride.**—These reagents could be mixed slowly or rapidly at 0° without evolution of hydrogen chloride. Kept at 0°, the mixture remained clear and colourless, and the slow production of *o*-chloroethylbenzene was not accompanied by evolution of hydrogen chloride. If the mixture was allowed to warm to 15° there occurred, after 1—1.5 hours, a rapid separation into two layers, accompanied by coloration and heat evolution, but still without evolution of hydrogen chloride. The lower layer was soluble in water, with evolution of much heat; the upper layer was insoluble. In none of the experiments with this hydroxy-compound was there any indication of the formation of phosphoric esters; all the phosphorus in the system was found in the aqueous solution after the aqueous treatment.

With the ( $-$ )alcohol (3.05 g., 1 mol.) and the stated amounts of oxychloride the following experiments were conducted.

(1) The alcohol ( $\alpha_D^{18}$  -18.8°) was quickly added to the oxychloride (1 mol.) at 0°, and after 5 minutes, the mixture on aqueous treatment yielded mainly unchanged alcohol.

(2) The mixture as in (1) was allowed to warm to 15°, and was given aqueous treatment after the separation into two layers; (+)*o*-chloroethylbenzene (1.15 g.), b. p. 78°/18 mm.,  $n_D^{15}$  1.5277,  $\alpha_D^{18}$  +3.6° (Found: Cl, 25.0. Calc.: Cl, 25.2%), and a very viscous residue (1.75 g.) were obtained. (3) When the mixture was kept at 0° for 9 hours, two layers were formed; after aqueous treatment (+)*o*-chloroethylbenzene (1.85 g.), b. p. 77°/16 mm.,  $\alpha_D^{18}$  +14.1° (from alcohol of  $\alpha_D^{18}$  -42.0°) (Found: Cl, 24.95%), and a viscous residue (1.14 g.) were obtained. The latter did not contain phosphorus. (4) With the alcohol ( $\alpha_D^{18}$  -42.0°) and oxychloride (0.5 mol.) at 0° for 9 hours, there was no separation; (+)*o*-chloroethylbenzene (2.0 g.),  $\alpha_D^{16}$  +19.5° (Found: Cl, 25.1%), and a residue (1.20 g.) were obtained. (5) The alcohol ( $\alpha_D^{18}$  -25.6°) and oxychloride (2 mols.) at 0° for 5 hours yielded, after aqueous treatment, (+)*o*-chloroethyl-

benzene (2.5 g.), b. p. 86°/25 mm.,  $\alpha_D^{18} + 5.2^\circ$  (Found: Cl, 25.1%) and a residue (0.5 g.). (6) With oxychloride (3 mols.) at 0° for 4 hours, (+)- $\alpha$ -chloroethylbenzene (1.7 g.),  $\alpha_D^{15} + 4.6^\circ$ , and a residue (1.2 g.) were formed.

*Interaction of (-)Phenylmethylethylcarbinol and Phosphorus Oxychloride in the Presence of Pyridine.*—The oxychloride was added dropwise to an ethereal solution of the alcohol (4.1 g., 1 mol.,  $\alpha_D^{18} - 18.8^\circ$ ) and pyridine (2.7 g., 1 mol.) at 0°. The separation of a white solid began immediately, and after an hour at 15°, this was filtered off, washed with dry ether, and the ethereal solution given aqueous treatment. Yields of  $\alpha$ -chloroethylbenzene, RCl, and the composition of the precipitates for different proportions of oxychloride are shown in the table.

POCl <sub>3</sub> , mols.	Ethereal solution.			White precipitate.			
	RCl, %.	$\alpha_D^{18}$ .	Cl, %.	G.	Cl, %.	P, %.	C <sub>5</sub> H <sub>5</sub> N, %.
0.37	40	+27.8°	24.95	4.0	17.1	9.5	51.0
0.72	45	+22.0	25.0	5.6	21.1	10.9	47.7
1.00	57	+18.0	25.2	6.35	26.6	11.2	42.2

Addition of oxychloride (1.03 g., 0.33 mol.) to the alcohol (2.44 g., 1 mol.) and pyridine (1.58 g., 1 mol.) in ethereal solution at -12° caused a very slow deposition of solid: for times up to 30 minutes, the amount of solid was small, and the yield of chloride 5%. The precipitate contained phosphorus, and the ratio Cl: C<sub>5</sub>H<sub>5</sub>N was consistently about 1:2. After 3 hours at -12°, a 25% yield of chloride,  $\alpha_D^{18} + 22.0^\circ$ , was obtained. When the reagents (alcohol of  $\alpha_D^{18} - 18.8^\circ$ ) were mixed rapidly in ethereal solution at 0°, and kept at this temperature for 2 hours before aqueous treatment, the results shown below were obtained: the composition of the precipitate is given in atomic or molecular proportions.

POCl <sub>3</sub> , mols.	C <sub>5</sub> H <sub>5</sub> N, mols.	RCl, yield %.	Cl, %.	$\alpha_D^{18}$ .	Proportions in precipitate.		
					Cl.	C <sub>5</sub> H <sub>5</sub> N.	P.
0.67	1	30	25.0	+27.5°	2.17	2.05	1
0.67	2	30	25.1	+35.5	2.1	2.4	1
1.0	2	47	25.3	+17.3	2.25	2.25	1

Finally, two experiments were conducted with the reagents mixed at 0° and then kept at 15° for 12 hours. The alcohol (3.66 g.,  $\alpha_D^{18} - 25.6^\circ$ , 1 mol.), the oxychloride (3.07 g., 0.67 mol.), and pyridine (4.8 g., 2 mols.) in ethereal solution formed a white precipitate (7.38 g.) (Found: Cl, 19.2; C<sub>5</sub>H<sub>5</sub>N, 46.3; P, 7.9%; Cl: C<sub>5</sub>H<sub>5</sub>N: P = 2.07:2.23:1), and (+)- $\alpha$ -chloroethylbenzene (1.9 g., 45%), b. p. 78°/16 mm.,  $\alpha_D^{18} + 63.0^\circ$ ,  $n_D^{20}$  1.5262 (Found: Cl, 24.9%). The aqueous washing of the decanted ethereal solution contained only traces of chloride and phosphate ions. In absence of ether, the alcohol (2.44 g.,  $\alpha_D^{18} - 42.1^\circ$ , 1 mol.), oxychloride (2.03 g., 0.67 mol.), and pyridine (3.2 g., 2 mol.) yielded (+)- $\alpha$ -chloroethylbenzene (1.9 g.), b. p. 80°/20 mm.,  $\alpha_D^{18} + 74.8^\circ$ ,  $n_D^{18}$  1.5270 (Found: Cl, 25.0%).

In none of the experiments described was there the slightest indication of the formation of phosphoric esters: the phosphorus content of each precipitate and aqueous washings of the ethereal solution accounted for all the phosphorus in the system.

*Interaction of Ethyl Mandelate and Phosphorus Oxychloride.*—Mixtures of mandelate (3 g., 1 mol.) and oxychloride (3 g., 1.1 mols.) were allowed to stand for the time and at the temperature stated in the table, and were then given aqueous treatment. A distillate of unchanged mandelate and a highly viscous residue, which did not contain phosphoric esters, were obtained in each experiment. Carbonate solutions yielded residues (0.2 g.) which also were phosphoric ester-free. Very little hydrogen chloride was evolved in these experiments.

Temp.	Time, hrs.	Distillate, ROH, g.,		Temp.	Time, hrs.	Distillate, ROH, g.,	
		b. p. 92—93°/3 mm.	Residue, g.			b. p. 92—93°/3 mm.	Residue, g.
15°	2	2.7	0.1	60°	4	0.75	1.65
40—50	2	1.3	0.95	65	5	— (POCl <sub>3</sub> , 2 mols.)	1.9
40—50	2.5	1.0	1.5				

*Interaction of Ethyl (-)Mandelate and Phosphorus Oxychloride in Presence of Pyridine.*—In ethereal solution, phosphorus oxychloride was added slowly to an ethereal solution of ethyl (-)mandelate (4.5 g., 1 mol.,  $\alpha_D^{18} - 130.1^\circ$ ) and pyridine (2 g., 1 mol.) at 0°. Precipitation of a white solid occurred immediately, but this was not simply pyridine hydrochloride, and some chloride, RCl, was formed at the same time. After 12 hours at 15° the solution was filtered and given aqueous treatment. Owing to the nearness of b. p.'s of ethyl mandelate and ethyl phenylchloroacetate, these were not separated; the chlorine content indicates the amount of the latter present (Calc.: Cl, 17.9%).

The residues were highly viscous gums containing phosphoric esters. Speed of mixing has significance, and affects the composition of the precipitate within 2—3 units in the percentages in experiments with constant amounts of reagents. Oxychloride (0.33 mol.) will precipitate nearly all the pyridine in the system in time; if, however, the rate of addition is such that the second third of a mol. is added before the first has completed its effect, the relative concentration of oxychloride is increased and this modifies the composition of the precipitate.

POCl <sub>3</sub> , mol.	Distillate, b. p. 92—93°/2—3 mm.,		Residue, g.	P, %.	Precipitate.				
	g.	Cl, %.			G.	Cl, %.	P, %.	C <sub>5</sub> H <sub>5</sub> N, %.	
0.33	1.0	13.9	+ 53.1°	2.9	5.5	4.45	16.5	3.4	42.2
0.66	2.6	17.0	+102.3	1.0	—	4.30	23.7	10.2	46.0
1.0	2.1	12.1	+ 43.6	0.4	—	4.72	22.9	11.2	42.3

In absence of ether, the oxychloride was added to the mandelate (3.0 g., 1 mol.,  $\alpha_D^{18} + 44.0^\circ$ ) and pyridine at 0°. Precipitation of a solid began immediately. After 24 hours at room temperature, the mixture was given aqueous treatment.

POCl <sub>3</sub> , mol.	C <sub>5</sub> H <sub>5</sub> N, mol.	Distillate, b. p. 92—93°/2—3 mm., g.		Cl, %.	$\alpha_D^{18}$ .	Residue, g.	P, %.
0.33	1	1.0		11.0	-12.4°	0.4°	4.2
						(0.65) *	
0.66	1	2.0		14.6	-19.2	0.45	—
1.0	1	2.5		17.9	-31.2	0.2	—
1.0	2	1.5		6.8	-3.2	0.2	—

\* From the carbonate solution.

The mandelate (3 g., 1 mol.) and oxychloride (5.12 g., 2 mols.) were mixed quickly at 15° (no evolution of heat), and then, after 4 hours at 65° and 1 hour at 65°/15 mm., the product was cooled to 0°, mixed with pyridine (2.62 g., 2 mols.), and the crystalline precipitate (3.332 g.) (Found : Cl, 21.6; P, 9.2;  $C_8H_8N$ , 42.5%) washed with dry ether. The residue from the ethereal solution did not yield any distillate, but left a dark red, highly viscous gum (1.8 g.).

The author expresses his thanks to the Chemical Society for a grant from the Research Fund, and to Dr. R. W. West for helpful discussions.

THE NORTHERN POLYTECHNIC, HOLLOWAY, LONDON, N. 7.

[Received, October 24th, 1944.]

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