Interaction of Carboxylic Acids with Phosphorus Trichloride, or Butyl Phosphorodichloridite, or the Chloridite in the Absence, and in the Presence of Pyridine.

By J. A. Cade and W. Gerrard.

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With acids such as acetic acid there was no evidence that chlorine attached to phosphorus in the trichloride or the phosphorochloridites could be replaced by an acyloxy-group by a primary reaction either in the absence or in the presence of pyridine, as it can be by an alkoxy-group. The primary reaction was the formation of acyl chloride. By a secondary reaction, and this only in the case of butyl phosphorodichloridite in the presence of pyridine, an acyl phosphite was obtained. However, benzoic acid, the trichloride, and pyridine immediately gave tribenzoyl phosphite on being mixed.

Correlation with the corresponding thionyl chloride systems is mentioned.

Little has been reported on the mechanism of the interaction of carboxylic acids and phosphorus trichloride, although the yields of acyl chlorides have been discussed (cf. Clark and Bell, *Trans. Roy. Soc. Canada*, 1933, **27**, III, 97; Bauer, *Oil and Soap*, 1946, **23**, 1). In many text-books the equation (1) is given; but in others equation (2) is favoured in order to allow for the formation of hydrogen chloride, which has also been attributed to reaction (3) (Lucas and Pressman, " Principles and Practice in Organic Chemistry," Wiley, New York, 1949, p. 267). Brooks (*J. Amer. Chem. Soc.*, 1912, **34**, 492) concluded that (1) was

$$(1)\quad 3R\cdot CO_2H + PCl_3 \longrightarrow 3R\cdot COCl + P(OH)_3$$
$$(2)\quad 3R\cdot CO_2H + 2PCl_3 \longrightarrow 3R\cdot COCl + P_2O_3 + 3HCl$$
$$(3)\quad CH_3\cdot CO_2H + PCl_3 \longrightarrow CH_3\cdot CO_2\cdot PCl_2 + HCl, \text{ etc.}$$

correct for the interaction of the acid and trichloride, but the reduced yield of acyl chloride and the evolution of hydrogen chloride were ascribed to reactions (4) and (5):

$$(4)\quad CH_3\cdot COCl + CH_3\cdot CO_2H \longrightarrow (CH_3\cdot CO)_2O + HCl$$
$$(5)\quad CH_3\cdot COCl + P(OH)_3 \longrightarrow P(OH)_2\cdot O\cdot CO\cdot CH_3 + HCl$$

The main point to be established is whether chlorine attached to tervalent phosphorus can be replaced by an acyloxy-group, and from experience with the corresponding alcohol systems, the reaction with dibutyl phosphorochloridite $PCl(OBu^n)_2$ in the presence of pyridine should be a crucial test (Gerrard, *J.*, 1940, 1464; Gerrard, Isaacs, Machell, Smith, and Wyvill, *J.*, 1953, 1920). Addition of the chloridite (1 mol.) to a solution of acetic acid (2 mols.) and pyridine (1 mol.) in pentane at −10° immediately afforded acetic anhydride (97% yield), dibutyl hydrogen phosphite (92%), and base hydrochloride. This result is considered to be due to the direct formation of acetyl chloride (1 mol.) and hydrogen phosphite, followed by interaction of the former and acetic acid (1 mol.) facilitated by the base (1 mol.) (Gerrard and Thrush, *J.*, 1952, 741; 1953, 2117). Only 1 mol. of the base was required, because, even if it took part in the first reaction, its availability for the second one would not be reduced by the neutral hydrogen phosphite. In the absence of pyridine, equimolecular proportions of chloridite and acid readily gave acetyl chloride (84%) and the hydrogen phosphite at 20°. But for the first result, this could be ascribed to the formation of acetyl dibutyl phosphite and the deacylation of it by hydrogen chloride as in the alcohol system: $PCl(OR)_2 + ROH \longrightarrow HCl + P(OR)_3 \longrightarrow O{:}PH(OR)_2 + RCl$. The other aliphatic acids examined behaved as acetic acid did.

Complications arose when butyl phosphorodichloridite was used. The dichloridite (1 mol.), acetic acid (2 mols.), and base (2 mols.) gave at 20° base hydrochloride, acetic anhydride (29%), and diacetyl butyl phosphite (44·6%). Butyl di*iso*butyryl phosphite and the dipropionyl compound were also obtained in a similar way. We believe that the acyl chloride was formed by a direct process as before, and that the other product, PCl(OH)·OR, decomposed to base hydrochloride and butyl metaphosphite, which with the anhydride formed diacyl butyl phosphite. Some support for this tentative suggestion is given by the fact that phosphorus trichloride and acid did not give acyl phosphite in the presence of base. About the intermediate phosphorus compounds mentioned, nothing appears to be known. We have not succeeded in preparing butyl metaphosphite, but by hydrolysing the dichloridite with the correct amount of water to form the compound PCl(OH)·OR in the presence of pyridine and acetic anhydride, we obtained base hydrochloride in almost theoretical yield and diacetyl butyl phosphite in 22·5% yield.

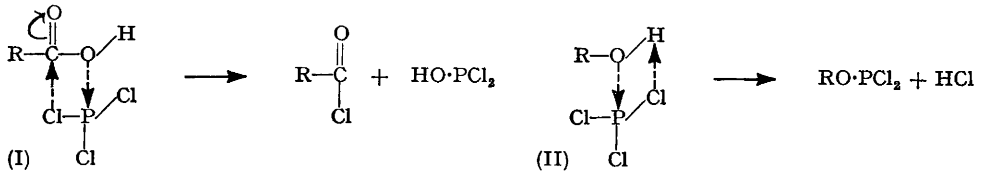
In the phosphorus trichloride–acid system we could find no evidence of R·CO·O–P bond formation, either in the absence or in the presence of base. We infer that two of the chlorine atoms readily cause direct formation of acyl chloride, equation (6) and (7), but

$$R{\cdot}CO_2H + PCl_3 \longrightarrow R{\cdot}COCl + PCl_2{\cdot}OH \quad (6)$$

$$R{\cdot}CO_2H + PCl_2{\cdot}OH \longrightarrow R{\cdot}COCl + PCl(OH)_2 \quad (7)$$

there can be complications over the third atom. From the yields of acyl chloride we conclude that the compound $PCl(OH)_2$ can continue to form acyl chloride, but some of it is degraded to hydrogen chloride and metaphosphorous acid. From the acid (3 mols.) and trichloride (1 mol.) at temperatures < 20° the yields of acyl chloride were acetyl 69, propionyl 72, *iso*valeryl 70%; and the residues contained from 36·4 to 42% of phosphorus [Calc. for $P(OH)_3$: P, 37·8%]. The loss of available chlorine can be compensated by providing more trichloride, but more than a small increase is a disadvantage in the examples of the lower members, because unchanged reagent interferes with purification of the acyl chloride. Clark and Bell (*loc. cit.*) do not mention having tried proportions other than trichloride (1·8 mols.) and acid (3 mols.) with which they obtained acetyl (79%), *n*-butyryl (68%), and *iso*hexanoyl (55%) chloride. For the preparation of chlorides of higher fatty acids (*e.g.*, stearic acid), Bauer (*loc. cit.*) used 1 mol. of trichloride to 1 of acid, 0·4 mol. of the former giving lower yields.

In the presence of pyridine a complication arose probably owing to the association of the base with the compound $PCl(OH)_2$. With ether or pentane as solvent there was a co-precipitation of base and reactive chlorine, so that with the reagents in the ratio $PCl_3 : 3CH_3{\cdot}CO_2H : 3C_5H_5N$, the yield of acetic anhydride was only 44%. To keep the chlorine available for formation of acyl chloride, and to ensure that there was enough pyridine to convert the acyl chloride into anhydride, we used chloroform as solvent and varied the proportions of reagents. With propionic acid (6 mols.), pyridine (4 mols.), and trichloride (1 mol.), the yield of anhydride was 92%. This result is in accord with the view that acyl chloride is formed by a direct process and then forms anhydride as described. Provisionally we depict this direct process as involving a four-centre transition state (I) but with a different orientation of reactive centres from that in the alcohol sytsem (II).



It is remarkable that benzoic acid (3 mols.), trichloride (1 mol.), and pyridine (3 mols.) gave base hydrochloride and tribenzoyl phosphite, obtained as a white solid. On the other hand, the acid reacted with thionyl chloride in the presence of pyridine as did acetic acid (Gerrard and Thrush, *loc. cit.*). Only one chlorine atom in thionyl chloride is available for formation of acyl chloride, the reaction apparently being similar to (I), the other product, SOCl·OH, decomposing to sulphur dioxide and hydrogen chloride. In the presence of pyridine, acyl chloride is formed in the same way; but the base and the compound SOCl·OH are both precipitated from ether or pentane. Consequently, 2 mols. of base are required for the conversion of 2 mols. of acid into anhydride by 1 mol. of thionyl chloride. Not even when butyl chlorosulphinate was used in the presence of pyridine was there any evidence of the formation of an acyl sulphite.

EXPERIMENTAL

Interaction of Acid (2 *Mols.*) *with Dibutyl Phosphorochloridite* (1 *Mol.*) *in the Presence of Pyridine* (1 *Mol.*).—The chloridite (10·63 g.) in pentane (25 c.c.) was added dropwise to a shaken solution of acetic acid (6·0 g.) and base (3·95 g.) in pentane (50 c.c.) at −10°; base hydrochloride (5·35 g.) was formed immediately. The filtrate gave acetic anhydride (4·95 g., 97%), b. p. 40—41°/11 mm. (Found: equiv., 51·8. Calc.: equiv., 51·0), dibutyl hydrogen phosphite (8·9 g., 92%), b. p. 130—133°/19 mm., n_D^{20} 1·4220 (Found: P, 15·8. Calc. for $C_8H_{19}O_3P$: P, 16·0%), and an undistillable glassy residue (1·0 g.) containing phosphorus (13·2%).

With *iso*butyric acid (8·8 g.), base hydrochloride (5·15 g.), *iso*butyric anhydride (7·0 g., 88·5%), b. p. 70—75°/11 mm. (Found: equiv., 79·7. Calc.: equiv., 79·0), a mixed fraction (0·5 g.), b. p. 105—120°/11 mm., dibutyl hydrogen phosphite (8·65 g., 89%), b. p. 125—130°/11 mm., n_D^{20} 1·4225 (Found: P, 15·5%), and an undistillable residue (1·4 g.) (Found: P, 12·0%) were obtained.

With *n*-heptanoic acid (12·0 g.), base hydrochloride (5·5 g.), a distillate (18·9 g.) with a long boiling range, and a residue (1·6 g.) were obtained. The distillate provided fractions from b. p. 70°/0·4 mm., n_D^{20} 1·4242 (Found: P, 12·0%), to b. p. 114°/0·4 mm., n_D^{20} 1·4331 (Found: P, 0·9%). It was not possible to separate dibutyl hydrogen phosphite, n_D^{20} 1·4215, and heptanoic anhydride, n_D^{20} 1·4340. All precipitates were good specimens of pyridine hydrochloride.

Benzoic acid (12·2 g.) behaved differently. Base hydrochloride weighed 3·8 g., and no hydrogen phosphite could be isolated. The distillates, b. p. 145—265°/0·005 mm., contained phosphorus, and on standing gave benzoic acid and benzoic anhydride. When benzoic acid (6·1 g., 1 mol.) in ether (total, 125 c.c.) was used, base hydrochloride weighed 5·1 g., but again the hydrogen phosphite could not be isolated. The behaviour on distillation indicated the presence of benzoyl dibutyl phosphite which was undergoing some decomposition to benzoic anhydride and polymerised material containing phosphorus. One fraction had b. p. 126—140°/0·01 mm., n_D^{20} 1·5032 (Found: P, 8·5%).

Acetic Acid and Dibutyl Phosphorochloridite.—The chloridite (10·63 g., 1 mol.) was quickly mixed with acetic acid (3·0 g., 1 mol.) in a flask which was immediately connected to an absorption tube (KOH) and shaken mechanically for 1 hr. at 20°. The absorption tube was replaced by a trap at −80°, followed by another absorption tube (KOH), and volatile matter was removed from the reaction vessel at 20°/1·0 mm. The two tubes contained but a trace of chloride ion. Trap contents (3·8 g.) gave acetyl chloride (3·3 g., 84%), b. p. 50—52° (Found: Cl, 46·3. Calc. for C_2H_3OCl: Cl, 45·2%). Residue (9·75 g.) in the reaction flask gave mainly dibutyl hydrogen phosphite, b. p. 91—93°/0·65 mm., n_D^{20} 1·4247 (Found: P, 15·0%), but it was not possible to free it completely from a chlorine compound by distillation.

Interaction of Butyl Phosphorodichloridite (1 *Mol.*) *with Acid* (2 *Mols.*) *and Pyridine* (2 *Mols.*).—The dichloridite (17·6 g.) in pentane (50 c.c.) was added dropwise to acetic acid (12·0 g.) and pyridine (15·8 g.) in pentane (250 c.c.) at −10°. A good specimen of base hydrochloride (23·25 g.) was formed during the mixing. From the filtrate, volatile matter was removed at 20°/0·1 mm. and collected at −80°, and from it acetic anhydride (3·0 g., 29·4%), b. p. 132—135°, was obtained. The primary residue (20·8 g.) afforded a fraction (0·95 g.), b. p. 75°/0·1 mm., n_D^{20} 1·4291, *diacetyl butyl phosphite* (9·9 g., 44·6%), b. p. 70—73°/0·07 mm., n_D^{20} 1·4261 (Found : C, 43·9; H, 7·0; P, 14·1. $C_8H_{15}O_5P$ requires C, 43·2; H, 6·75; P, 13·9%), a fraction (1·65 g.), b. p. 80—110°/0·1 mm. (decomp.), and a residue (4·3 g.) (Found : P, 23·3%). After being kept at 15° for 14 days, the acetyl phosphite gave a range of fractions, the main fraction (4·8 g.) having b. p. 76—79°/0·4 mm., n_D^{20} 1·4352 (Found : P, 14·5%). In a trap at −80° placed between the receiver and the pump trap, acetic anhydride (0·8 g.) was collected.

Similarly from *iso*butyric acid (8·95 g., 2 mols.) and pyridine (7·9 g., 2 mols.), base hydrochloride (11·2 g.), *iso*butyric anhydride (3·9 g., 48·5%), b. p. 170—176° (Found : equiv., 80·3. Calc. : equiv., 79·0), n-*butyl di*iso*butyryl phosphite* (4·6 g., 33%), b. p. 80—84°/0·07 mm., n_D^{20} 1·4279 (Found : C, 51·0; H, 8·0; P, 11·0. $C_{12}H_{23}O_5P$ requires C, 51·8; H, 8·3; P, 11·15%), a fraction (1·05 g.), b. p. 114—118°/0·4 mm., n_D^{20} 1·4332, and an undistillable residue (2·25 g.) (Found : P, 18·2%) were obtained.

Similarly, propionic acid (7·4 g., 2 mols.) afforded base hydrochloride (11·5 g.), propionic anhydride (2·3 g., 35·4%), b. p. 152—154° (Found : equiv., 65·5. Calc. : equiv., 65·0), *butyl dipropionyl phosphite* (6·3 g., 50·4%), b. p. 84—88°/0·01 mm., n_D^{20} 1·4377 (Found : P, 12·3. $C_{10}H_{19}O_5P$ requires P, 12·4%), and an undistillable residue (2·2 g.) (Found : P, 15·1%).

With the intention of forming butyl metaphosphite (believed to be responsible for the diacyl phosphite) in a different way, the dichloridite (8·8 g., 1 mol.) was added rapidly to acetic anhydride (20·5 g.) at −10°. A mixture of pyridine (7·9 g., 2 mols.) and water (0·9 c.c., 1 mol.) was then added. After 1 hr., ether (200 c.c.) was added. The insoluble matter (11·0 g.) was a good specimen of base hydrochloride. Evaporation at 20°/0·1 mm. afforded ether, acetic anhydride (17·3 g.), and a residue which gave diacetyl butyl phosphite (2·5 g., 22·5%), b. p. 67—70°/0·09 mm., n_D^{20} 1·4255 (Found : P, 14·1%).

Acid and Phosphorus Trichloride.—The trichloride (11·46 g., 1 mol.) was added to acetic acid (15 g., 3 mols.) at 20°, and the mixture was shaken for 2 hr. Two layers separated immediately, and only 0·003 g.-ion of chlorine was held in the alkali trap which followed the trap kept at −80°. Volatile matter was removed at 20°/15 mm. (1 hr.), and after being warmed to 50°/0·05 mm. during 1 hr. the residue weighed 6·0 g. (Found : P, 42·0. Calc. for H_3O_3P : P, 37·8%). The contents of the cold trap were distilled, a cold trap, followed by the existing alkali trap, being attached to the receiver. Hydrogen chloride (total, 0·48 mol.), acetyl chloride (13·5 g., 69%), b. p. 50—52° (Found : Cl, 46·0. Calc. : Cl, 45·2%), and acetic acid contaminated with hydrogen chloride were isolated. In another experiment acetyl chloride (70% yield), b. p. 50—52°, d_4^{20} 1·105 (Found : Cl, 45·1%), and a residue (Found : P, 40·8%) were obtained.

Similarly, propionic acid (18·5 g., 3 mols.) and trichloride (1 mol.) afforded hydrogen chloride (0·62 mol.) and acyl chloride (16·7 g., 72%), b. p. 75—77° (Found : Cl, 39·2. Calc. for C_3H_5OCl : Cl, 38·4%). *iso*Valeric acid (10·2 g.) afforded the chloride (8·4 g., 70%), b. p. 114—115° (Found : Cl, 29·5. Calc. for C_5H_9OCl : Cl, 29·5%), and a residue (6·62 g.) (Found : P, 36·4%). A mixture of unchanged acid and some anhydride accounting for about 10% of total acid was obtained. During the reaction at 20° the hydrogen chloride evolved was only 0·04 mol.

Interaction of Propionic Acid with Phosphorus Trichloride in Presence of Pyridine.—The trichloride (11·46 g., 1 mol.) in pentane (50 c.c.) was added dropwise to a solution of the acid (37·35 g., 6 mols.) and pyridine (39·5 g., 6 mols.) in pentane (200 c.c.) at −10°. The precipitate (33·0 g.) (Found : $Cl : C_5H_5N : P = 2{\cdot}91 : 2{\cdot}76 : 0{\cdot}63$) was formed immediately, and from the filtrate volatile matter was removed at 20°/15 mm. The residue (52·0 g.) gave impure acid (6·7%), b. p. 135—140° (Found : equiv., 75·2. Calc. for $C_3H_6O_2$: equiv., 74·0), a mixture of acid and anhydride (1·5 g.), b. p. 140—158°, propionic anhydride (24·0 g., 73%), b. p. 158—160°, and a residue which at 0·1 mm. gave a further 12% of anhydride. The final residue weighed 3·2 g. (0·03 mol.) (Found : P, 28·0%).

As the pyridine compounds in this system are soluble in chloroform, reactions were carried out in this solvent. The yield of anhydride never exceeded 88%, some acid was always recovered and no evidence of the formation of acyl phosphites could be secured. It appeared that pyridine was not urgently required for the formation of the intermediate acyl chloride, but would probably have the effect of reducing the reactivity of the postulated intermediate $PCl(OH)_2$. We therefore reduced the proportion of base to 3 mols; but this was too drastic, for the phosphorous acid then withheld pyridine from the anhydride reaction. The yield of anhydride was 68%, and some acid and acyl chloride were present. The optimum amount of base was about 4 mols. Trichloride (11·46 g., 1 mol.) was added to the acid (6 mols.) and pyridine (4 mols.) in chloroform (250 c.c.). Removal of volatile matter at 20° (low pressure) gave a residue (43 g.) (Found : Cl : C_5H_5N : P = 2·72 : 3·24 : 0·99) which contained all the phosphorus. The trapped distillate afforded anhydride (30·0 g., 92%), b. p. 158—162° (Found : equiv., 66·0. Calc. for $C_6H_{10}O_3$: equiv., 65·0), and a mixture of acid and anhydride.

Interaction of Benzoic Acid and Phosphorus Trichloride in the Presence of Pyridine.—Benzene proved to be a better solvent than ether. The trichloride (2·3 g., 1 mol.) in benzene (5 c.c.) was added dropwise to a solution of benzoic acid (6·1 g., 3 mols.) and pyridine (3·95 g., 3 mols.) in benzene (30 c.c.) at 0°. A good specimen of base hydrochloride (5·65 g., 98%) (Found : Cl, 30·2; C_5H_5N, 67·1. Calc. for C_5H_6NCl : Cl, 30·7; C_5H_5N, 68·4%) was immediately formed, and the filtrate gave *tribenzoyl phosphite* (6·32 g., 96%), m. p. 93—95° (Found : P, 7·8. $C_{21}H_{15}O_6P$ requires P, 7·9%). This compound (3·7 g.) gave on distillation at 0·1 mm. benzoic anhydride (1·1 g.), b. p. 40—41°/0·1 mm. (Found : equiv., 112·6. Calc. : equiv., 113·0), and a glassy residue (2·0 g.) (Found : P, 13·2%).

Butyl phosphorodichloridite (8·8 g., 1 mol.) in benzene (50 c.c.) was added to a solution of benzoic acid (12·2 g., 2 mols.) and pyridine (7·9 g., 2 mols.) in benzene (300 c.c.) at 20°. A good specimen of base hydrochloride (10·4 g.) (Found : Cl, 30·4; C_5H_5N, 67·6%) was immediately formed. Evaporation of the solvent afforded a residue (19·1 g.) which could be neither crystallised nor distilled. It was thoroughly degassed at 40°/0·05 mm. (Found : P, 8·4. Calc. for $C_{18}H_{19}O_5P$: P, 9·0%).

Materials.—All solvents were dried, and reagents were distilled just before use. Butyl phosphorodichloridite was prepared as described by Gerrard (*loc. cit.*) and dibutyl phosphorochloridite as described by Gerrard *et al.* (*J.*, 1953, 1920).

Dr. A. M. Thrush prepared the tribenzoyl phosphite.

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