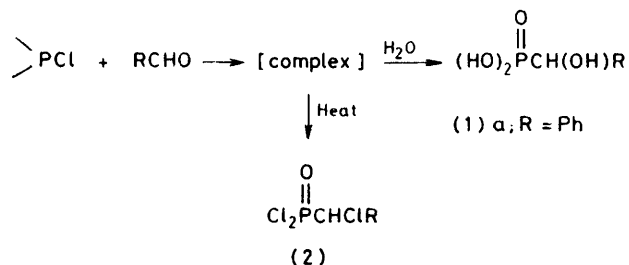# Reactions of Carbonyl Compounds with Tervalent Phosphorus Reagents. Part 11.[1] A Re-examination of the Reaction of Benzaldehyde with Phosphorus Trichloride in the Presence of Acetic Anhydride

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The reaction of equimolar amounts of benzaldehyde, phosphorus trichloride, and acetic anhydride has been shown to involve successive formation of benzylidene diacetate (4) and α-chlorobenzyl acetate (5). By an Arbusov reaction, the latter is converted into the dimer (3), previously recognised as the precursor of α-hydroxybenzyl-phosphonic acid (1a), the known product of an aqueous work-up. A simple preparation of α-chlorobenzyl acetate (5) is described.

THE reactions of halogenophosphines with aldehydes have attracted almost a century of attention from organic chemists. In general, the outcome of these reactions is the formation of a new carbon–phosphorus bond, and increased co-ordination of phosphorus, as shown in Scheme 1. The earliest work in the area was that of

$$ \diagdown \!\!\! P Cl \; + \; RCHO \longrightarrow [\text{complex}] \xrightarrow{H_2O} (HO)_2 \overset{\overset{\displaystyle O}{\|}}{P} CH(OH)R $$

(1) a; R = Ph

$$ \downarrow \text{Heat} $$

$$ Cl_2 \overset{\overset{\displaystyle O}{\|}}{P} CHClR $$

(2)

SCHEME 1

Fossek,[2] who reported the transformation of aldehydes and phosphorus trichloride into α-hydroxyalkyl phosphonates (1) via an aqueous reaction work-up. Similar observations were later recorded by Michaelis[3a] and Page.[3b] Then came a series of papers by J. B. Conant's group,[4] the objectives of which were partly mechanistic. However, these reactions proved to be too difficult for the techniques then available, and a decade of effort left many questions unanswered.

One of the problems of this work was that either acetic acid or acetic anhydride was usually used as co-solvent, but the effect of these additives was never properly established. This situation was not changed by the later efforts of Atherton et al.,[5] although the fundamental role of the phosphorus trichloride as an electrophilic entity was now better understood. Meanwhile, Kabachnik and Shepeleva[6] went back to the simpler two-component systems, and confirmed that the phosphorus trichloride functioned as an electrophile, and that the purely thermal reaction generally yields an α-chloroalkylphosphonic dichloride (2) (Scheme 1).

These efforts, however, provided no real indication of the intermediates involved in reactions of this type, far less any information on the overall reaction sequence. To some extent, this situation was improved by recent work[7] using phosphorus trichloride and simple aldehydes. Systems involving a further additive, like acetic anhydride, remain something of a mystery, and the

object of this paper is to describe experiments which clarify the role of acetic anhydride in these reactions.

In this study, we have concentrated on the three-component system benzaldehyde–acetic anhydride–phosphorus trichloride, partly because this was quite the best characterised system and partly because of the sequence of clean reactions found to occur at reasonable rates at room temperature. The earlier work of Conant et al.[4a,4d] and Atherton et al.[5] indicated that an equimolar mixture of the three reactants gives acetyl chloride, and a tacky syrup which is left after evaporation of the acetyl chloride. The latter workers also showed that this oil could be converted into an amorphous solid, which was assigned structure (3), and whose formation was suggested to be the result of the sequence shown in Scheme 2. Our work has confirmed the formation of

$$ PhCHO \; + \; PCl_3 \longrightarrow PhCH(Cl)OPCl_2 \xrightarrow{Ac_2O} $$

$$ \longleftarrow PhCH(OAc)PCl_2 $$

(3)
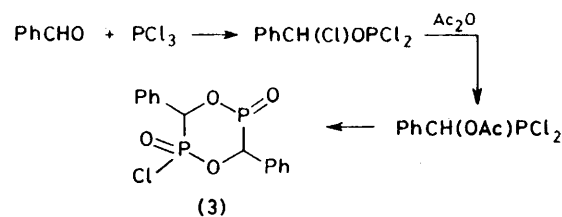
SCHEME 2

this solid, and, moreover, shows that it can be precipitated as it forms in the reaction medium, when light petroleum is used as solvent.

RESULTS AND DISCUSSION

A [1]H n.m.r. study of the sequence of reactions leading to (3) was therefore undertaken. This revealed that all the aldehyde was consumed within 1 h, as was the anhydride. Subsequently, work with [^{2}H$_5$]benzaldehyde confirmed that the initial product was benzylidene diacetate (4), since the single benzylic proton could now be detected (δ 7.8) and its integrated value obtained. Thereafter, the absorptions due to (4) diminished, to be replaced, after 3 h, by equal concentrations of acetyl chloride and α-chlorobenzyl acetate (5). During the remainder of the reaction, α-chlorobenzyl acetate (5) is steadily consumed, until only acetyl chloride absorptions remain outside the aromatic region.

This sequence of reactions is outlined in Scheme 3. It

is so different from any previous suggestions that a few comments are appropriate. The formation of 1,1-diacetates from aldehydes is a well known reaction,[8] but it normally requires an acid catalyst. We have shown that phosphorus trichloride is necessary for this conversion, and that its function is purely catalytic.[9] This is in contrast with earlier views, in which phosphorus trichloride was held to be linked to the aldehyde during the first stage of the sequence. The second stage, leading to α-chlorobenzyl acetate (5), is clearly an ester-halogen exchange, of a type now familiar from the work of Gazizov et al.[10] Independent experiments with pure (4) also resulted in the clean formation of α-chlorobenzyl acetate (5) on reaction with phosphorus trichloride. This ester is a surprisingly rare compound, until recently only available in poor yield.[11] Provided due care is taken, we find [12] that (5) can be prepared directly from benzaldehyde and acetyl chloride. This enabled us not only to check the identity of the proposed intermediate, but also to investigate the chemistry of (5) independently.
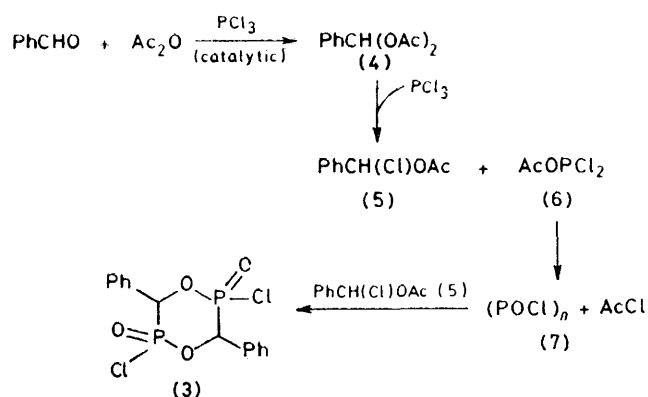
SCHEME 3

In the original three-component reaction, the formation of α-chlorobenzyl acetate (5) should, by stoicheiometry, be accompanied by the formation of acetoxy-(dichloro)phosphine (6). This is clearly not stable under the reaction conditions, since acetyl chloride ultimately provides the only methyl absorption, other than that due to (5). We therefore looked at other ways of generating (6), and investigated the reaction of acetic anhydride with phosphorus trichloride, a reaction described [4a] as being very slow at temperatures below 50 °C. In our hands, an equimolar mixture of these two substances completely reacted in 16 h at 20 °C, to produce equal amounts of acetyl chloride, and at least two acetates. N.m.r. signals due to the latter slowly disappear over a week, leaving acetyl chloride as the major (>95%) absorption. Any attempt to heat the mixture simply accelerates the above sequence dramatically. This experiment confirmed the instability of acetoxy(dichloro)phosphine (6), and we suggest that it eliminates acetyl chloride to give $(POCl)_n$, (7), a polymer, as shown in Scheme 3. The species $(POCl)_n$ was previously described in the benzaldehyde–phosphorus trichloride reaction.[7]

It thus seems reasonable to assume that the original three-component reaction produces a mixture of α-chlorobenzyl acetate (5) and the polymer (7) after the first few hours. Their expected reactivity was demonstrated by mixing samples of each, prepared separately, and following, by [1]H n.m.r., their reaction at 20 °C. Once 50% of the α-chlorobenzyl acetate (5) has been consumed, addition of light petroleum to the mixture produces a white solid, which is the same dimer (3) as that formed in the original reaction. We suggest that these observations can be explained by assuming that the polymer (7) contains phosphorus in the three-co-ordinate state, and that (7) possesses sufficient nucleophilicity to perform an Arbusov-type reaction with the ester (5) (see Scheme 3). The reaction of benzaldehyde with phosphorus trichloride is believed to proceed by a similar reaction, using benzal chloride in the phosphorus-carbon bond-forming step.[7] In the present case, the Arbusov reaction proceeds at 20 °C, whereas in the benzaldehyde–phosphorus trichloride reaction it requires heating to 150 °C, and this presumably reflects the greater reactivity of α-chlorobenzyl acetate (5), as compared with benzal chloride. As with the earlier study, there are no detectable intermediates in the final stages, and the exact details of formation of (3) are not apparent from the present data.

As for the cyclic dimer (3), we have found it to be every bit as intractable as the literature suggests. On prolonged storage, or on the least contact with moisture, it forms a sticky resin, and it took a good deal of experimental perseverance to achieve its isolation as a solid in the first instance.

The present work therefore provides an explanation for the role of acetic anhydride in diverting the benzaldehyde–phosphorus trichloride reaction into a new pathway, leading ultimately to a slightly different product, i.e. (3). In essence, these pathways are simply ways of generating aldehyde-derived alkylating agents, in the presence of the polymeric species (7), a mildly nucleophilic reagent. A consequence of this interpretation is that any notion of aldehyde–phosphorus(III) halide reactions proceeding via oxaphosphiran intermediates,* as originally suggested by Page [3b] and Conant et al.,[4a,d] must now be discarded.

EXPERIMENTAL

Reaction of Phosphorus Trichloride, Benzaldehyde, and Acetic Anhydride.—(a) *In light petroleum as solvent.*

* These have been the focal point of discussion of several important organophosphorus reactions [notably the Perkow reaction leading to enol phosphorus(IV) esters] which require the transformation of P–C–O structures into P–O–C structures.

Benzaldehyde (3.18 g, 0.03 mol) and acetic anhydride (3.06 g, 0.03 mol) were mixed in dry light petroleum (b.p. 40—60 °C) (50 ml) in a flask under nitrogen. Phosphorus trichloride (4.11 g, 0.03 mol) was added over 10 min, *via* a syringe and serum-cap, to the stirred solution. After 1.5 h at 20 °C, the stirred mixture became cloudy, and a white solid began to precipitate. Stirring was continued for 17 h, and the solid removed by filtration of the mixture in a nitrogen atmosphere. After washing with a little light petroleum–ether (10 : 1), the powder [8.21 g, 73% based on structure (3)] was fine, white, and free-flowing. Upon storage, or the least exposure to air, it darkened and became tacky, and ultimately a syrup. The powder had no definite m.p., and seemed to dissolve only in solvents with which it reacted, or which were wet.

(b) *In deuteriochloroform.* The same solutes (0.003 mol) as in (a) were dissolved in deuteriochloroform (1 ml) and the homogeneous mixture stirred at 20 °C for 16 h. Analysis by ^{1}H n.m.r. showed that both the aldehyde and the anhydride had been consumed within 45 min, to give absorptions at δ 2.05 (s, OAc) and 7.8 (s, PhC*H*). After 3 h these absorptions had disappeared, and had been replaced by new absorptions at δ 2.18 (s, OAc) and 2.6 (s, AcCl). Thereafter the absorption at δ 2.18 diminished steadily, and by 16 h the only observable non-aromatic absorption was due to acetyl chloride. Removal of volatile material yielded acetyl chloride, identified by i.r. and ^{1}H n.m.r. The residual material was a sticky resin (0.75 g), which was dissolved in dry chloroform (2 ml). Addition of light petroleum (b.p. 40—60 °C) and trituration yielded a white amorphous solid (0.61 g, 89%), which had the same properties as that described in (a).

Reaction of Pentadeuteriobenzaldehyde with Phosphorus Trichloride and Acetic Anhydride.—Pentadeuteriobenzaldehyde [13] (0.111 g, 0.001 mol), acetic anhydride, (0.102 g, 0.001 mol), and phosphorus trichloride (0.137 g, 0.001 mol) were dissolved in deuteriochloroform, and the mixture kept sealed at 20 °C under nitrogen. Successive ^{1}H n.m.r. spectra showed the complete formation, after 0.5 h, of [^{2}H$_5$]benzylidene diacetate [δ 7.8 (s, 1 H) and 2.05 (s, 6 H)], then, after 2 h, of α-chloro[^{2}H$_5$]benzyl acetate [δ 7.5 (s, 1 H) and 2.18 (s, 3 H)] and finally, after 24 h, of acetyl chloride [δ 2.6 (s)]. At the end of this period, no absorption other than that due to acetyl chloride, was detectable.

Reaction of Benzylidene Diacetate with Phosphorus Trichloride.—Benzylidene diacetate (2.10 g, 0.01 mol) and phosphorus trichloride (1.38 g, 0.01 mol) were mixed together under nitrogen. As the diacetate dissolved, the mixture warmed up appreciably, and a small sample of the mixture was removed and taken up in deuteriochloroform (0.4 ml). ^{1}H N.m.r. spectroscopy showed that the diacetate had reacted completely within 2 h at 20 °C, to give α-chlorobenzyl acetate and acetyl chloride, as above. After 24 h, there was a very weak absorption at δ 6.72 (d, *J* 4.5 Hz), and another at δ 1.98 (s), as well as a strong absorption due to acetyl chloride. Removal of volatile material from the bulk reaction yielded a viscous syrup, from which a white powder (0.97 g) was obtained as above. The ^{1}H n.m.r. assignments were confirmed by a similar reaction (0.001 mol scale) of [^{2}H$_5$]benzylidene diacetate in deuteriochloroform.

Preparation of α-Chlorobenzyl Acetate (5).—This experiment was conducted under the most rigorously dry conditions. Failure in this respect resulted in either no reaction, or a low conversion into (5). Freshly distilled acetyl chloride (7.8 g, 0.1 mol) and benzaldehyde (10.6 g, 0.01 mol) were

mixed in dry, redistilled chloroform (20 ml). After 4 h at 20 °C, the aldehyde was fully reacted, and removal of the solvent left a mobile liquid, which was fractionally distilled to give α-chlorobenzyl acetate (5) [12] (11.0 g, 61.5%), b.p. 88—89 °C at 1.5 mmHg; *m/e* 186 and 184 (M^+), 149, 106, 102, 100, 80, and 78; $\nu_{max.}$ (film) 2 950, 1 775s, 1 212, 835, and 705 cm^{-1}; δ_H 2.10 (3 H, s, OAc) and 7.3—7.8 (6 H, m, Ph and C*H*Cl). The main fraction was usually preceded by a little acetyl chloride, then a little benzaldehyde.

Reaction of Acetic Anhydride with Phosphorus Trichloride.—Acetic anhydride (1.53 g, 0.015 mol) and phosphorus trichloride (2.06 g, 0.015 mol) were stirred at 20 °C under nitrogen in a small flask. After 16 h, ^{1}H n.m.r. indicated that acetyl chloride (δ 2.66, s) had formed, and that its integrated intensity was the same as that of several acetate absorptions (δ 2.2—2.4) taken together. Very slowly the latter absorptions declined, until after one week acetyl chloride accounted for *ca.* 95% of the original acetic anhydride. When the mixture was opened to the atmosphere a fairly rapid darkening of the liquid occurred, and when the mixture was heated, in an attempt to distil the products, charring resulted.

Reaction of α-Chlorobenzyl Acetate (5) *with* (POCl)$_n$.—α-Chlorobenzyl acetate (1.82 g, 0.01 mol) was added *via* a syringe and serum cap to acetyl chloride (0.78 g, 0.01 mol). The mixture was kept at 20 °C for one week, but no evidence of any reaction was obtained (^{1}H n.m.r.).

α-Chlorobenzyl acetate (1.82 g, 0.01 mol) was then added, in a separate experiment, to a mixture of acetic anhydride (1.02 g, 0.01 mol) and phosphorus trichloride (1.37 g, 0.01 mol) which had already been stirring for one week, and which was shown to be 95% converted into acetyl chloride, and, presumably, (POCl)$_n$. The homogeneous mixture was stirred for 24 h, by which time *ca.* 50% of the acetate (5) had reacted (relative to the acetyl chloride). Dry light petroleum (b.p. 40—60 °C) (20 ml) was gradually added to the mixture and a white solid (0.95 g) precipitated. This solid had the same properties as that isolated (above) from the reaction of acetic anhydride, benzaldehyde, and phosphorus trichloride.

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