

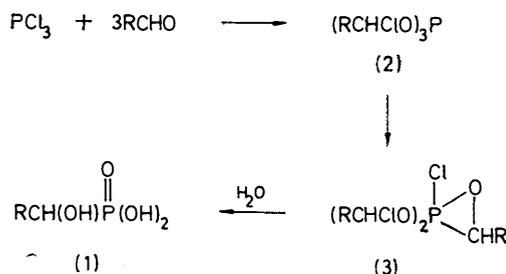
Reactions of Carbonyl Compounds with Tervalent Phosphorus Reagents. Part V.¹ Aldehydes and Phosphorus Trichloride

By J. Allen Miller* and M. John Nunn, Department of Chemistry, The University, Dundee DD1 4HN

The reaction of phosphorus trichloride with aldehydes has been reinvestigated, and the formation of bis-1-chloroalkyl ethers and 1,1-dichloroalkanes at moderate temperatures is described. The *gem*-dichlorides are direct precursors of the thermal reaction products, α -chloroalkylphosphonic dichlorides. A reaction scheme is presented in which phosphorus trichloride is depicted as a typical electrophilic halide in the initial stages of the reaction. The results of several previous studies of these reactions may now be rationalised.

HALOGENOPHOSPHINES are extremely reactive,² and are characterised by an ability to act either as electrophiles or as nucleophiles. Thus, in reactions with groups possessing both potentially nucleophilic and electrophilic centres, establishment of reaction pathways can be difficult. This is the situation with simple carbonyl compounds, such as aldehydes, whose reactions with halogenophosphines have been studied for nearly a century, with almost every decade witnessing fresh structural or mechanistic work.

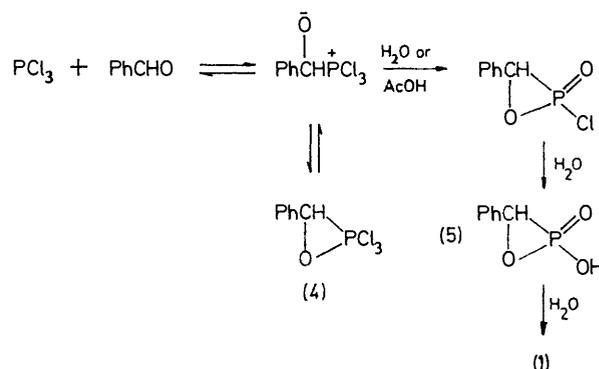
The earliest significant work on aldehyde-phosphorus trichloride reactions was by Fossek³ and Page;⁴ this was followed by a series of studies by Conant's group.^{5,6} Their results are summarised in Schemes 1 and 2,



SCHEME 1

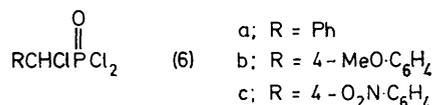
respectively. In essence, the achievement of Fossek³ was the isolation and characterisation of the products after aqueous work-up as α -hydroxyphosphonic acids (1), believed⁴ to be formed *via* the phosphite (2) and the oxaphosphiran (3). The Harvard group was able to

isolate a phosphonic acid intermediate, claimed to have structure (5), and to be formed *via* the oxaphosphiran (4).



SCHEME 2

Kabachnik and Shepeleva^{7,8} later showed that pyrolysis of aldehydes with phosphorus trichloride gives α -chloroalkylphosphonic dichlorides (6), believed to be derived by an Arbusov-type reaction of the phosphite (2). Kabachnik thus viewed⁸ phosphorus trichloride as



acting as an electrophile towards the aldehyde carbonyl oxygen atom, in agreement with Fossek and Page, but

⁵ J. B. Conant and A. D. Macdonald, *J. Amer. Chem. Soc.*, 1920, **42**, 2337.

⁶ J. B. Conant and V. H. Wallingford, *J. Amer. Chem. Soc.*, 1924, **46**, 192.

⁷ M. I. Kabachnik and E. S. Shepeleva, (a) *Doklady. Akad. Nauk S.S.S.R.*, 1950, **75**, 219; (b) *Izvest. Akad. Nauk S.S.S.R.*, 1950, 39.

⁸ M. I. Kabachnik, *Russ. Chem. Rev.*, 1947, **16**, 402.

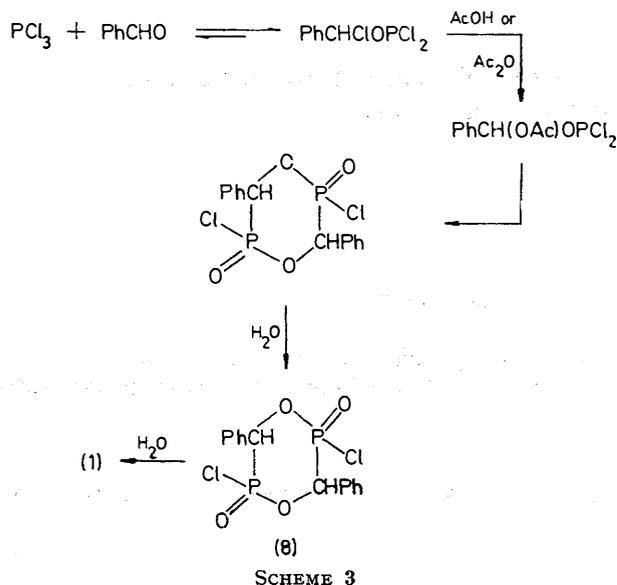
¹ Part IV, J. Iball, P. Kaye, and J. A. Miller, *J.C.S. Perkin II*, 1974, 650.

² For general discussion of halogenophosphine reactivity see B. J. Walker, 'Organophosphorus Chemistry', Penguin, London, 1972, pp. 67, 72-76.

³ W. Fossek, *Monatsh.*, 1884, **5**, 627; 1886, **7**, 20.

⁴ H. J. Page, *J. Chem. Soc.*, 1912, **101**, 423.

in contrast to Conant. Support for the former view then came from the work of Atherton *et al.*,⁹ who provided chemical evidence for the intermediacy of the phosphorodichloridite (7) in the reaction with benzaldehyde, although (7) was not isolated and purified. They also repeated Conant's isolation of the species (5), showed that it should be represented as a cyclic dimer (8), and furthermore suggested that (8) might be formed from its acid chloride, as in Scheme 3.



At the outset of the work described here, it seemed that there was scope for a closer look at these reactions, especially those conducted under conditions where the basic aldehyde-trichloride reaction could be studied on its own. While the reactivity of phosphorus trichloride is generally agreed to be electrophilic,¹⁰ the lack of isolable pre-hydrolysis intermediates in previous work made the various mechanistic implications, discussed above, largely unsupported. Furthermore, although the identity of the species (5) had been questioned,⁹ there was room for further evidence, in view of the debate¹¹ about the existence of oxaphosphiran rings in intermediates or transition states in several important organophosphorus reactions.

Our strategy was to examine the reactions of phosphorus trichloride with simple aldehydes under mild conditions which might allow the accumulation of intermediates. Thus benzaldehyde was kept under nitrogen at room temperature for 3–5 days in the presence of an equimolar amount of phosphorus trichloride, after which all the aldehyde was consumed.¹² This was demonstrated by ¹H n.m.r., which also showed a new singlet at τ 2.95, accounting for over 95% of the original aldehyde. When this reaction was repeated

with two moles of benzaldehyde to one of phosphorus trichloride, the aldehyde was again completely consumed, although if three moles were used not quite all the aldehyde signal disappeared.

When the sealed equimolar mixture was heated to 70 °C for a few hours, the τ 2.95 singlet diminished, that due to the aldehyde reappeared, and a new singlet was observed at τ 3.3. After further heating to 100 °C, the aldehyde singlet was completely removed, and the τ 3.3 singlet was then the only non-aromatic signal. When the product was distilled, benzylidene chloride was isolated in good yield; this was responsible for the τ 3.3 signal. Further heating of other samples brought to this stage in the reaction showed that at temperatures beyond 160 °C the phosphonic dichloride (6a) was produced smoothly and efficiently, as expected.^{7b}

Repetition of this sequence with [²H₅]benzaldehyde showed that other intermediates with n.m.r. signals obscured by the phenyl ring protons had not accumulated at any stage of the reaction leading to (6). Moreover, it was also clear that the loss of the signal at τ 2.95 led to the production of benzaldehyde and benzylidene chloride in almost equal amounts although the aldehyde signal subsequently diminished fairly rapidly. The stoichiometry of this regeneration of benzaldehyde suggested that the unknown intermediate might be bis- α -chlorobenzyl ether (9a). Attempts to isolate the ether were not successful, owing to its sensitivity to heat under the reaction conditions, and its apparent instability to aqueous work-up. A literature survey revealed no authentic case of its preparation and isolation, although the related *p*-nitrobenzyl ether (9b) has been reported¹³ from a reaction of *p*-nitrobenzaldehyde with phosphorus pentachloride.

We therefore turned our attention to *p*-substituted benzaldehydes in the hope of confirming the formation of bis-ethers, and, moreover, of obtaining information on aromatic substituent effects on the reaction rate. No reaction of *p*-nitrobenzaldehyde with phosphorus trichloride in deuteriochloroform was observed at room temperature, and even at 100 °C in dioxan the reaction was extremely sluggish. However we were able to isolate the bis-ether (9b) from this reaction, and to confirm its structure by comparison with a sample prepared from phosphorus pentachloride.¹³ By contrast the related reaction with *p*-methoxybenzaldehyde was extremely rapid, and indeed yielded (α -chloro-*p*-methoxybenzyl)phosphonic dichloride (6b) as the main product at room temperature.

Acetaldehyde reacted vigorously with phosphorus

⁹ F. R. Atherton, V. M. Clark, and A. R. Todd, *Rec. Trav. chim.*, 1950, **69**, 295.

¹⁰ B. E. Ivanov and V. F. Zheltukhin, *Russ. Chem. Rev.*, 1970, **39**, 358.

¹¹ For recent work which has centred on the question of three-membered rings see F. Ramirez, *Accounts Chem. Res.*, 1968, **1**, 168; Y. Ogata and M. Yamshita, *J. Amer. Chem. Soc.*, 1970, **92**, 4670; *Tetrahedron*, 1971, **27**, 2725; V. M. Clark, P. Chopard, R. F. Hudson, and A. J. Kirby, *Tetrahedron*, 1965, **19**, 1961; A. N. Pudovik, I. V. Konovalova, V. P. Kakurina, and V. A. Fomin, *J. Gen. Chem. (U.S.S.R.)*, 1974, **44**, 249; A. N. Pudovik, I. V. Guryanova, and S. P. Perebezentseva, *ibid.*, 1969, **39**, 2364.

¹² Preliminary communication, J. A. Miller and M. J. Nunn, *Tetrahedron Letters*, 1972, 3953.

¹³ A. Kliegl and K. Haas, *Ber.*, 1909, **42**, 2587.

poor yields^{7a} of phosphonic dichlorides (6), obtained by using aliphatic aldehydes other than formaldehyde, or by using certain *p*-substituted aromatic aldehydes, such as the *p*-nitro-compound.

Our work has not thrown light on the steps which lead to the bis-ethers (9), beyond a general confirmation of the initial electrophilic role of phosphorus trichloride, and a rationalisation of the observation³ that three moles of aldehyde react with one of the trichloride to produce a water-sensitive intermediate from which aldehyde may be regenerated by hydrolysis. Although the 1:1 adduct (7) discussed by Atherton *et al.*⁹ remains an attractive possibility, our work does not provide any firm evidence for this. The reactions of phosphorus trichloride studied by Conant's group were carried out in the presence of additives, such as water, acetic acid, or acetic anhydride, and it now seems likely that these have a fundamentally different pathway from those described here.

EXPERIMENTAL

I.r. spectra were run on a Perkin-Elmer 157 G spectrometer, and n.m.r. spectra on a Perkin-Elmer R10 instrument at 60 MHz, with tetramethylsilane as internal standard. All liquid reagents were freshly distilled prior to use and all reactions were performed under nitrogen. *p*-Nitrobenzaldehyde was purified by crystallization from chloroform.

Reactions of Benzaldehyde with Phosphorus Trichloride.—

(A) 1:1 Ratio. (a) *At 200 °C.* Benzaldehyde (12.6 g, 0.12 mol) and phosphorus trichloride (16.5 g, 0.12 mol) were heated in a Carius tube sealed under nitrogen to 200 °C for 2.5 h. The product was extracted with chloroform (50 ml), the solvent evaporated, and the residue distilled to give α -chlorobenzylphosphonic dichloride (6a) (9.3 g, 32%), b.p. 157–160 °C at 0.2 mmHg, m.p. 60–61 °C (lit.,^{7b} 60–61 °C); ν_{\max} , 1260 cm⁻¹; τ 2.2–2.8 (5 H, m) and 4.60 (1 H, d, *J* 6.1 Hz).

(b) *At room temperature.* A mixture of reagents as in (a) was stirred for 80 h, by which time the aldehyde had been totally consumed, as shown by the loss of aldehyde ¹H n.m.r. absorption. In addition to the aromatic signals, a new peak (singlet at τ 2.95) had appeared. When water was added to the mixture, benzaldehyde (62%) was recovered. Attempts to distil volatile material from further mixtures (brought to the stage when no aldehyde remained) yielded only starting materials, together with benzylidene chloride, in various proportions. The mixture before distillation showed ³¹P n.m.r. peaks at –42.5, –39.5, and –218.7 (PCl₃) p.p.m. downfield from 85% phosphoric acid.

(c) *At 70 °C.* Benzaldehyde (0.187 g, 0.0018 mol) and phosphorus trichloride (0.244 g, 0.0018 mol) were weighed into an n.m.r. tube, which was sealed under nitrogen after addition of deuteriochloroform as solvent. The tube was heated at 70 °C, and the aldehyde signal at τ 0.00 diminished fairly rapidly to be replaced by the absorption at τ 2.95 and a further singlet at τ 3.30. After 24 h at 70 °C, the only signal outside the aromatic region was that at τ 3.30. When this experiment was repeated on a larger scale (0.1 mol), careful distillation of the residue yielded benzylidene chloride, b.p. 105–107 °C at 12 mmHg (lit.,²⁰ 207 °C at 756 mmHg) in 92% yield. Comparison of the

n.m.r. spectrum of benzylidene chloride with that of the mixture after 24 h at 70 °C showed no detectable difference.

(d) *At 180 °C.* Benzaldehyde and phosphorus trichloride in a sealed n.m.r. tube as in (c) were heated at 180 °C for 36 h; the signal due to benzylidene chloride (τ 3.30) had then almost disappeared. The major absorption was due to α -chlorobenzylphosphonic dichloride (τ 4.60) (equivalent to ca. 85% of the starting aldehyde).

(e) *With [²H₅]benzaldehyde.* [²H₅]Benzaldehyde (0.224 g, 0.002 mol) and phosphorus trichloride (0.275 g, 0.002 mol) were stirred under nitrogen at room temperature. The gradual appearance of the singlet at τ 2.95 was observed (94% after 10 days) but no other intermediate absorption was detected. When the mixture was heated to 50 °C, [²H₅]benzaldehyde and [²H₅]benzylidene chloride were formed. The ratio of the integrals for their singlet absorptions reached 0.85:1.0, and thereafter diminished as the sample was warmed to 70 °C.

(B) 2:1 Ratio. Benzaldehyde (1.06 g, 0.01 mol) and phosphorus trichloride (0.69 g, 0.005 mol) were stirred together for 1 week. Analysis by n.m.r. showed that the aldehyde was totally consumed, and the only non-aromatic absorption appeared at τ 2.95. Raising of the temperature to 70 °C resulted in formation of benzylidene chloride after 24 h.

(C) 3:1 Ratio. Benzaldehyde (1.59 g, 0.015 mol) and phosphorus trichloride (0.69 g, 0.005 mol) were stirred at room temperature for 1 week. Analysis by n.m.r. showed that some benzaldehyde remained (12%), and that the remainder had been converted into the compound absorbing at τ 2.95. Heating this mixture to 70 °C produced the same change as in (B).

[²H₅]Benzaldehyde.—This was prepared from [²H₆]benzene, aluminium chloride, and 1,1-dichloromethyl methyl ether in methylene chloride.²¹ Yields, after distillation, varied from 9 to 23%. The product showed only an aldehyde singlet at τ 0.00 in its n.m.r. spectrum.

Reaction of [²H₅]Benzaldehyde with Thionyl Chloride.—Thionyl chloride (0.135 g, 0.0011 mol) was added to [²H₅]benzaldehyde (0.237 g, 0.0022 mol) in an n.m.r. tube, and the mixture was shaken thoroughly after sealing the tube. The mixture was kept at room temperature for 18 days, successive n.m.r. spectra showed a gradual reduction in the aldehyde absorption (48% reacted), and the formation of bis- α -chloro[²H₅]benzyl ether (9a) (36%) and [²H₅]benzylidene chloride (12%). The composition of this mixture did not change over the last 5 days. A careful augmentation experiment with bis- α -chloro[²H₅]benzyl ether and [²H₅]benzylidene chloride, each prepared separately from phosphorus trichloride and [²H₅]benzaldehyde, showed exact matching of the absorptions. Further heating of the mixture to 40 °C resulted in greater amounts of [²H₅]benzylidene chloride.

Reaction of *p*-Nitrobenzaldehyde with Phosphorus Trichloride.—(a) *At room temperature.* *p*-Nitrobenzaldehyde (3.02 g, 0.02 mol) and phosphorus trichloride (2.75 g, 0.02 mol) were stirred as a slurry at room temperature for 5 days, but no reaction was observed. Addition of chloroform (15 ml) to the mixture, followed by further stirring for 5 days, produced no change.

(b) *At 100 °C in dioxan.* A mixture as in (a) was dissolved in dry dioxan (10 ml) at 100 °C and maintained at

²⁰ 'Dictionary of Organic Compounds,' Eyre and Spottiswoode, London, 1965, vol. 2, p. 1001.

²¹ A. Rieche, H. Gross, and E. Hoft, *Chem. Ber.*, 1960, **93**, 88.

this temperature for 40 h, by which time some aldehyde still remained (30%), and new singlet n.m.r. absorptions were observed at τ 2.74 (66%) and 2.88 (<5%). The mixture was then poured into water (50 ml) and the pale orange precipitate was filtered off, washed with ether-acetone (1:1), and recrystallized from acetone. The solid was bis- α -chloro-*p*-nitrobenzyl ether (9b) (1.12 g, 31.5%), m.p. 166–170 °C (lit.,¹³ 170 °C) (Found: C, 47.2; H, 3.0; Cl, 20.2; N, 7.75. Calc. for C₁₄H₁₀Cl₂N₂O₅: C, 47.05; H, 2.8; Cl, 19.85; N, 7.85%); τ (dioxan) 1.62 and 2.15 (4 H, dd, *J* 8.6 Hz) and 2.74 (1 H, s); ν_{\max} 1 610, 1 515, 1 340, 1 085, and 700 cm⁻¹.

*Reaction of p-Nitrobenzaldehyde with Phosphorus Pentachloride.*¹³—Finely powdered phosphorus pentachloride (30.5 g, 0.146 mol) was added to *p*-nitrobenzaldehyde (21.0 g, 0.139 mol) cooled to 0 °C. The solid mixture was stirred rapidly and after 2 min an exothermic reaction ensued and the mixture became liquid. Next day the mixture was poured onto iced water (400 ml) and washed with aqueous sodium hydrogen carbonate (10%; 300 ml). A pale yellow oil separated and crystallized after 1 h to give bis- α -chloro-*p*-nitrobenzyl ether (9b) (2.3 g, 13%), m.p. 168–170 °C. The filtrate was extracted with ether (2 × 75 ml); the extract, washed with water (2 × 50 ml), yielded *p*-nitrobenzylidene chloride (16.5 g, 58%), m.p. 44–45 °C (lit.,¹³ 46 °C); τ (dioxan) 1.67 and 2.18 (4 H, dd, *J* 8.6 Hz) and 2.90 (1 H, s); ν_{\max} 1 604, 1 530, 1 350, 877, 824, and 718 cm⁻¹.

Reaction of p-Methoxybenzaldehyde with Phosphorus Trichloride.—*p*-Methoxybenzaldehyde (6.8 g, 0.05 mol) was run into phosphorus trichloride (7.35 g, 0.05 mol) cooled to 0 °C and stirred gently. The mixture was allowed to come to room temperature slowly, and then stirred for 24 h, after which the aldehyde was wholly consumed. Analysis by n.m.r. showed a new absorption at τ 4.54 (d, *J* 5.0 Hz) due to α -chloro-*p*-methoxybenzylphosphonic dichloride (60%). Attempted distillation under vacuum resulted in charring.

Reaction of Acetaldehyde with Phosphorus Trichloride.—Phosphorus trichloride (3.4 g, 0.025 mol) was slowly dripped through a reflux condenser into a solution of acetaldehyde (6.6 g, 0.15 mol) in dry benzene (40 ml) at 0 °C. The stirred mixture was allowed to come to room temperature, and stirred for a further 12 days. Successive n.m.r. spectra indicated that paraldehyde was the only initial product, but that it was slowly converted into bis-1-chloroethyl ether (9d). By this time the mixture had turned black, and fractional distillation yielded only traces of bis-1-chloroethyl ether, identified by comparison with a sample prepared from thionyl chloride, and acetaldehyde.

The reaction took the same course when solvent was omitted, and the resultant black tar did not yield any bis-ether.

*Reaction of Acetaldehyde with Thionyl Chloride.*¹⁷—Thionyl chloride (23.8 g, 0.2 mol) was slowly dripped onto acetaldehyde (17.6 g, 0.4 mol) which was cooled to 0 °C and stirred vigorously. After the initial exothermic reaction had subsided, the mixture was warmed to 50 °C for 1 h and then stirred at room temperature overnight. Distillation yielded bis-1-chloroethyl ether (9d) (75%).

*Pyrolysis of Bis- α -chloro-*p*-nitrobenzyl Ether (9b).*—The ether (0.5 g) was heated to 170 °C for 40 min. The resulting dark brown liquid solidified on cooling. Analysis of the mixture by n.m.r. and t.l.c. (chloroform) indicated partial decomposition of the ether and formation of *p*-nitrobenzaldehyde and *p*-nitrobenzylidene chloride (5:2).

Pyrolysis of Bis-1-chloroethyl Ether (9d).—A solution of the ether (0.5 g) in deuteriochloroform (0.5 ml) was sealed in an n.m.r. tube and heated at 145 °C for 4 h. No reaction was detected by n.m.r.

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