

Reactions of Carbonyl Compounds with Tervalent Phosphorus Reagents. Part VI.¹ Benzoate Esters and Halogenophosphines

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Chloro(di-*t*-butyl)phosphine reacts with alkyl benzoates to give phosphine oxides, alkyl chlorides, and aroyl chlorides. Kinetic and other evidence is presented for a mechanism involving rate-determining, competing nucleophilic attack by the phosphine at the alkyl and carbonyl carbon atoms of the esters. Reactions of methyl diphenylphosphinite with benzoyl and acetyl chlorides are discussed, and the products are related to addition reactions of acyldiphenylphosphine oxides.

ALKYL benzoates (1a and b) have previously been shown to be dealkylated on heating with chlorodiphenylphosphine (2a), to give an alkylidiphenylphosphine oxide (3), an aroyl chloride (4), and an alkyl chloride (5).² The isolation of benzoyl chloride and the oxide (3a or b) in similar yields was taken as evidence that they were both formed by initial attack at the alkyl group of (1a or b) by chlorodiphenylphosphine (2a) (path a in Scheme 1); the alkyl chloride (5) was believed to result from attack by (2a) at the carbonyl group of the ester (path b).

However, distinction between the pathways shown in Scheme 1, and other reasonable alternatives² such as rate-determining nucleophilic attack by an ester (1) on a halogenophosphine (2), was tentative, and partly based on the fact that the ester (1c) reacted twice as rapidly as the ester (1a).² Another unsatisfactory feature of the earlier work was that aroyldiphenylphosphine oxides (6) were never isolated from these reactions, despite the fact that the overall stoichiometry of the dealkylations suggested that they were formed.² This paper is concerned with both these aspects of the previous work, and describes dealkylation reactions with chloro(di-*t*-butyl)phosphine (2b), and attempts to prepare benzoyldiphenylphosphine oxide (6a).

Chloro(di-*t*-butyl)phosphine (2b) was found to react

with methyl benzoate (1a) at 180 °C over 30 h, and to form products analogous to those observed² for (1a) and (2a) at 180 °C. The isolated yields of benzoyl chloride (54%) and di-*t*-butyl(methyl)phosphine oxide (3c) (57%) were similar, and methyl chloride (5a) was detected in lesser amounts (37%), along with traces of isobutene. Thus whereas chlorodiphenylphosphine (2a) showed a preference for attack at the carbonyl group of (1a), the more hindered chloro(di-*t*-butyl)phosphine (2b) reacted more slowly and predominantly at the methyl group.

When these studies were extended to benzyl benzoate (1c), the picture was less clear, since the major product was dibenzyl-(*t*-butyl)phosphine oxide (7) [64% based on ester (1c)], and benzoyl chloride (38%) and a small yield of benzyl(di-*t*-butyl)phosphine oxide (3d) were also isolated. Clearly two benzyl groups had been added to the phosphorus of (2b), and the 'missing' *t*-butyl group was accounted for by the formation of isobutene (52%). It seems likely that the loss of isobutene occurs from a phosphonium intermediate, and there is precedent for this.³ Phosphonium intermediates have been described previously in halogenophosphine-ester reactions,² and the isobutene loss might occur from a salt such as (8), giving benzylchloro-(*t*-butyl)phosphine (9), which could be benzylated by further reaction with the starting benzyl ester (Scheme 2). It is not possible, however, to

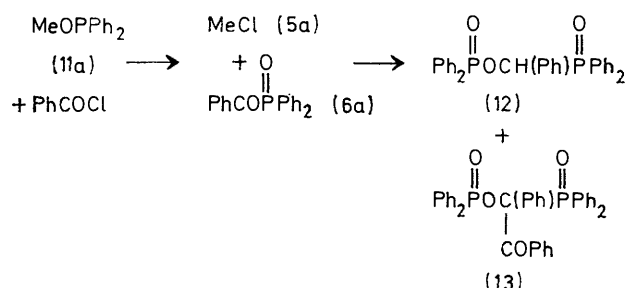
¹ Part V, J. A. Miller and M. J. Nunn, *J.C.S. Perkin I*, 1976, 535.

² S. T. McNeilly and J. A. Miller, *J. Chem. Soc. (C)*, 1971, 3007.

³ A. P. Stewart and S. Trippett, *J. Chem. Soc. (C)*, 1970, 1263.

a necessary step to explain the formation of an alkyl-diphenylphosphine oxide (3).

We therefore examined the reaction of methyl diphenylphosphinite (11a) with benzoyl chloride (4a) and found it to be extremely vigorous, even at 0 °C, with or without solvent. The initial reaction released copious amounts of methyl chloride (5a) almost instantaneously, and a red-orange colouration was observed. When the reaction was performed under nitrogen in the absence of solvent, this colouration persisted as long as the mixture was undisturbed, and an i.r. spectrum showed a band at 1650 cm⁻¹. This was presumably due to benzoyldiphenylphosphine oxide (6a),* formed as shown in Scheme 4. Addition of solvent, such as dry ether, to the red mixture resulted in rapid loss of colour, until the mixture was a very pale cream colour, by which time a copious white precipitate had formed. This was shown to consist of a mixture of [α -(diphenylphosphinyloxy)benzyl]diphenylphosphine oxide (12) and [α -benzoyl- α -(diphenylphosphinyloxy)benzyl]diphenylphosphine oxide (13), both of which have been described.⁶ The isolation of oxides such as (12) from attempted preparations of acyldiphenylphosphine oxides has been observed several times,⁶⁻⁹ and their formation is believed^{8,9} to result from reaction of adventitious water with the acylphosphine oxide, to produce diphenylphosphine oxide (14), which then adds to the carbonyl group of the acylphosphine oxide. However a recent study⁵ of the



SCHEME 4

deliberate hydrolysis of the oxide (6a) indicates that the oxygen of water attacks not at phosphorus but at the carbonyl carbon atom in (6a). Thus the origin of the second phosphorus group in the oxides (12) and (13) is not clear, and the problem appears to require further study.

The related reaction of methyl diphenylphosphinite (11a) with acetyl chloride was found to take a similar course. The main products were the oxides (15) and (17), which have been described,⁸ and n.m.r. evidence was obtained that the oxide (16) was also formed,

* This oxide has been described, but not isolated.⁵ This work was published after our study was completed, and describes an essentially identical route to benzoyldiphenylphosphine oxide.

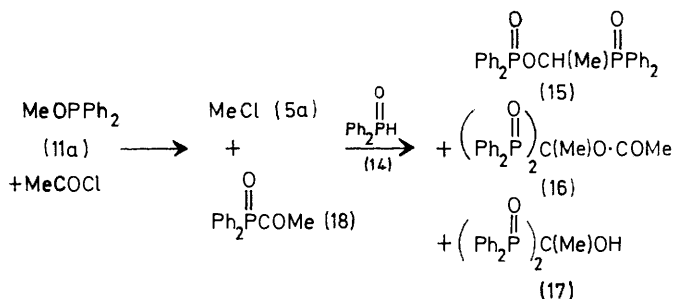
⁵ C. Brown, R. F. Hudson, and R. G. Searle, *Phosphorus*, 1973, **2**, 287.

⁶ R. S. Davidson, R. A. Sheldon, and S. Trippett, *J. Chem. Soc. (C)*, 1967, 1547.

⁷ K. Issleib and E. Priebe, *Chem. Ber.*, 1959, **92**, 3183.

⁸ R. S. Davidson, R. A. Sheldon, and S. Trippett, *J. Chem. Soc. (C)*, 1968, 1700.

although we were not able to separate (15) and (16). Once again these products seem to have arisen by further



reaction of an acylphosphine oxide, in this case acetyl-diphenylphosphine oxide (18). These observations suggest that the reactivity of α -oxo-phosphoryl compounds is greatest for the diphenylphosphine oxides, such as (6a) and (18), since the corresponding dialkylphosphine oxides^{3,10} are isolable, as are the related phosphonates.¹¹

These experiments are significant on two counts to the results of the ester dealkylations discussed above. First they demonstrate the great reactivity of benzoyldiphenylphosphine oxide (6a), and suggest that its isolation from reactions at 180 °C would be most unlikely. Furthermore, in the presence of benzoyl chloride, the alkyl diphenylphosphinites, e.g. (11a), would probably not survive long enough to be isomerized to alkyl-diphenylphosphine oxides (3). Isomerizations of this type are well known,¹² but usually require more vigorous conditions than do the acylation reactions of phosphinites described above. On balance, it would seem that Scheme 3 is unlikely to be the route to the main products of the benzoate dealkylations, and that the sequence shown in Scheme 1 still provides the best available rationalisation of the kinetic and structure-reactivity data discussed in this and earlier papers.²

EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer 137 spectrometer, and n.m.r. spectra on a Perkin-Elmer R-10 spectrometer. The benzoates, either purchased or synthesized by standard methods, were redistilled before use, as was chlorodiphenylphosphine. The phosphine oxides were purified by column chromatography on silica gel (May and Baker) and identified by comparison with samples prepared independently. Chloro(di-*t*-butyl)phosphine¹³ and methyl diphenylphosphinite⁵ were made by standard methods and stored under nitrogen. All reactions were performed in dry conditions, under nitrogen.

*Reaction of Chloro(di-*t*-butyl)phosphine (2b) with Methyl Benzoate.*—Chloro(di-*t*-butyl)phosphine (3.6 g, 2×10^{-2} mol) and methyl benzoate (2.72 g, 2×10^{-2} mol) were

⁹ E. Lindner, H. D. Ebert, and P. Junkes, *Chem. Ber.*, 1970, **103**, 1364.

¹⁰ Y. Ogata and H. Tomioka, *J. Org. Chem.*, 1970, **35**, 596.

¹¹ K. Sasse, in 'Methoden der Organischen Chemie' (Houben-Weyl), Thieme, Verlag, Stuttgart, 1963, vol. 12/1, p. 454.

¹² These have been reviewed by V. Mark, in 'Mechanisms of Molecular Migrations', ed. B. S. Thyagarajan, Wiley-Interscience, New York, 1969; and by L. A. Hamilton and P. S. Landis in 'Organic Phosphorus Compounds', ed. G. M. Kosolapoff and L. Maier, Wiley-Interscience, New York, 1972, vol. 4, p. 491.

¹³ W. Voskuil and J. F. Arens, *Org. Synth.*, 1968, **48**, 47.

sealed in a dry Carius tube under nitrogen and the tube was heated at 180 °C for 48 h. Fractional distillation of the residue yielded benzoyl chloride (1.5 g, 54%), b.p. 40–43 °C at 1.5 mmHg, identified by its i.r. spectrum, and di-*t*-butyl(methyl)phosphine oxide (3c) (2.0 g, 57%), b.p. 74–75 °C at 1.5 mmHg; τ 8.65 (3 H, d, J 10 Hz, MeP) and 8.72 (18 H, d, J 13.5 Hz, Bu^tP). A sample of (3c), prepared by treatment of (2b) with methyl-lithium, then hydrogen peroxide, gave identical data.

When the same reaction (1×10^{-3} mol scale) was repeated in a sealed n.m.r. tube, it was found that all the methyl benzoate had reacted after 30 h. As the contents of the tube were cooled to 0 °C, a strong signal at τ 7.2 (s) for methyl chloride² was observed, along with a small absorption for isobutene (τ 5.3 and 8.3). Both absorptions disappeared when the tube was opened and left in the n.m.r. preheater for 1 h. The weight loss due to evaporation of the methyl chloride (18 mg) was compatible with an estimate of the methyl chloride yield (37%) by n.m.r. integration. The signal assignments for methyl chloride and isobutene were checked by careful addition of each gas to the opened n.m.r. tube at 0 °C.

Reaction of Chloro(*di-t*-butyl)phosphine (2b) with Benzyl Benzoate.—This experiment was carried out as above (scale 2×10^{-2} mol) at 180 °C. The n.m.r. spectrum of the crude product showed that no ester remained, and the most notable features were absorptions at τ 6.70 and 6.80 (each d, each J 11 Hz). Distillation yielded benzoyl chloride, b.p. 62–65 °C at 6 mmHg (0.95 g, 38%), identified by its i.r. spectrum.

The residue was chromatographed with ether as solvent. Early fractions were traces of red oily material, but methanol-ether (1 : 50) eluted a series of fractions which contained varying proportions of the materials responsible for the τ 6.7–6.8 absorptions. These were separated by fractional crystallization from petroleum (b.p. 60–80 °C), since the major component was much less soluble than the minor one. The insoluble material was identified as dibenzyl(*t*-butyl)phosphine oxide (1.8 g, 64% based on the benzyl ester), m.p. 156–158 °C (lit.,³ 159–162 °C), τ 2.70 (10 H, s), 6.95 (4 H, d, J 12 Hz), and 8.9 (9 H, d, J 14 Hz). The mother liquor yielded, after further recrystallization from petroleum (b.p. 60–80 °C), benzyl(*di-t*-butyl)phosphine oxide (55 mg, 1.3%), m.p. 110–113 °C (lit.,³ 115–117 °C), τ 2.7 (5 H, s), 6.88 (2 H, d, J 11 Hz), and 8.8 (18 H, d, J 14 Hz).

Repetition of this experiment in a sealed n.m.r. tube (scale 1×10^{-3} mol) revealed that reaction was complete in 40 h, and that isobutene (52%) was a component of the product mixture. The isobutene was identified as in the previous experiment, and the yield calculated and checked similarly—it is quoted on the basis that 1 mol of chloro(*di-t*-butyl)phosphine can give 1 mol of isobutene.

Reaction of Methyl *p*-Cyanobenzoate with Chloro(*di-t*-butyl)phosphine. This was carried out exactly as for the corresponding reaction of methyl benzoate. Distillation yielded *p*-cyanobenzoyl chloride (1.7 g, 51%), and methyl-di-*t*-butylphosphine oxide (2.1 g, 60%). Analysis of an n.m.r. tube reaction (scale 10^{-3} mol) revealed that methyl chloride (30%) and isobutene (7%) were also formed.

In a further experiment, chloro(*di-t*-butyl)phosphine (0.180 g, 10^{-3} mol), methyl benzoate (0.136 g, 10^{-3} mol), and methyl *p*-cyanobenzoate (0.161 g, 10^{-3} mol) were sealed under nitrogen in an n.m.r. tube. The methoxy-absorptions of the esters were distinguishable at τ 6.10 and 6.17

(methyl benzoate) and the results of integration [comparison with the *t*-butyl absorptions (τ 8.85)] were as expected. The mixture was heated for 28 h at 190 °C, at which time the ester methoxy-signals had ceased to decline. Integration (comparison with the aromatic signals) showed that reaction had resulted in loss of methyl benzoate (8%) to a much lesser extent than methyl *p*-cyanobenzoate (94%), and that methyl-di-*t*-butylphosphine oxide (76%) and methyl chloride (20%) were the major products. Traces of isobutene were also detected by n.m.r. (in yields below 5%).

Reactions between Methyl Diphenylphosphinite and Benzoyl Chloride.—(a) *With no solvent.* Benzoyl chloride (1.4 g, 0.01 mol) was added dropwise to methyl diphenylphosphinite (2.16 g, 0.01 mol) stirred under nitrogen at 0 °C. A rapid and vigorous exothermic reaction occurred, with simultaneous development of a strong red colour in the mixture and evolution of methyl chloride. Analysis by i.r. showed complete loss of the C=O absorption due to benzoyl chloride, and an intense new band at 1 650 cm⁻¹. The thick oily product could not be induced to form crystals, but its colour and consistency did not alter with time. When the oil was triturated with ether (anhydrous or otherwise) the colour faded, first to yellow, then to off-white, and a copious crystalline precipitate was formed. T.l.c. in ether-ethanol (25 : 1) indicated that two components were present, with similar R_F values. The mixture was then chromatographed on silica in benzene-chloroform (4 : 1), and a white crystalline solid was eluted with this solvent. After two recrystallizations from ethanol-benzene (1 : 1), this solid was identified as α -benzoyl- α -(diphenylphosphinyloxy)benzyl-diphenylphosphine oxide (13) (10–20% yield), m.p. 208–210 °C (lit.,⁶ 207–208 °C) (Found: C, 74.35; H, 5.0; P, 9.8. Calc. for C₃₈H₃₀O₄P₂: C, 74.5; H, 4.9; P, 10.1%); ν_{\max} (Nujol) 1 680 (C=O), 1 268, 1 245 (P=O), 1 200 and 1 192 (P=O), 1 110, 1 025, and 864 cm⁻¹; m/e 612, 395, 217, 201, and 105. The ¹H n.m.r. spectrum showed complex multiplets in the aromatic region.

Further chromatography, with chloroform as solvent, yielded the second component. After repeated crystallization from benzene-ether this was identified as [α -(diphenylphosphinyloxy)benzyl]diphenylphosphine oxide (12) (32–40% yield), m.p. 199–200 °C (lit.,⁶ 190–191 °C) (Found: C, 72.85; H, 5.35; P, 12.35. Calc. for C₃₁H₂₆O₃P₂: C, 73.2; H, 5.1; P, 12.2%); ν_{\max} (Nujol) 1 220 (ester P=O), 1 205 (oxide P=O), 1 135, 1 118, 1 015, 996, and 840 cm⁻¹; m/e 508, 307, 217, and 201; τ 2.1–3.0 (25 H, m) and 3.7 (1 H, dd, J_{PH} 11 and 2 Hz).

In further similar experiments direct chromatography of the oily product yielded the same two oxides, (13) and (12). Attempted distillation of the crude oil *in vacuo* resulted in gradual loss of colour and the collection of a pale yellow oily distillate. When dissolved in organic solvents this was found to consist of a mixture of (13) and (12) (t.l.c.).

When methyl diphenylphosphinite was added to either equimolar or five-fold excess amounts of benzoyl chloride, the same oxides were formed. The temperature did not appear to be critical, since the reaction at the reflux temperature of benzoyl chloride gave the same crude products.

(b) *In organic solvents.* Benzoyl chloride (1.4 g, 0.01 mol) dissolved in sodium-dried ether was added dropwise to a stirred solution of methyl diphenylphosphinite (2.16 g, 0.01 mol) in dry ether under nitrogen. A pale yellow colouration was observed during the addition, but this faded slowly, as a white precipitate formed. After stirring

for a further 15 min, the mixture was filtered, and the residue (2.1 g) found (t.l.c.) to consist of the oxides (13) and (12). Similar experiments at 0 and -78°C gave similar results.

Reaction of Methyl Diphenylphosphinite with Acetyl Chloride.—Acetyl chloride (1.70 g, 0.022 mol) was added dropwise to methyl diphenylphosphinite (4.32 g, 0.02 mol) stirred under nitrogen at 0°C . The mixture rapidly turned yellow and methyl chloride was evolved steadily. The thick oily yellow product did not solidify on removal of unchanged acetyl chloride (traces) under nitrogen *in vacuo*, but was decolorized almost instantaneously on addition of ether, and white crystals were formed. The crystals were removed; t.l.c. [benzene–chloroform (5:1)] showed three components, the more mobile two of which were only just resolved (other solvents failed to separate these compounds). Column chromatography on silica (same solvent) gave three main fractions.

The first was an oil (0.4 g), identified as 1-diphenylphosphinyl-1-diphenylphosphinyloxyethane (15); τ 2.0–3.1 (20 H, m), 3.5 (1 H, m), and 8.5 (3 H, dd, J_{HH} 7, J_{PH} 14 Hz); ν_{max} (film) 1235 and 1200 cm^{-1} (P=O). The second was also an oil (0.9 g), tentatively identified as 1,1-bisdiphenylphosphinylethyl acetate (16); τ 2.1–2.9 (m), 7.85 (s, acetate), and 7.95 [t, J_{PH} 15 Hz, $\text{MeC}(\text{O}:\text{P}(\text{C}_6\text{H}_5)_2)_2$]. Despite repeated chromatography, this oil did not crystallize, probably owing to the presence of small amounts ($<5\%$ by n.m.r. and t.l.c.) of (15). The third component was 1,1-bisdiphenylphosphinylethanol (17), m.p. $159\text{--}160^{\circ}\text{C}$ (lit.,⁸ $159\text{--}160^{\circ}\text{C}$) (2.4 g); τ 2.0–3.1 (21 H, m) and 8.5 (3 H, t, J_{PMe} 15 Hz); ν_{max} (mull) 1212, 1185, 1122, 1115, 907, and 805 cm^{-1} .

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