

Reactions of Carbonyl Compounds with Tervalent Phosphorus Reagents Part 9.¹ Benzaldehyde with Phosphinites in the Presence of Acetic Acid

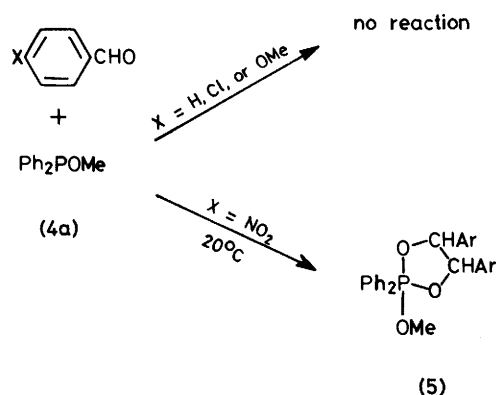
By J. Allen Miller* and Denis Stewart, Chemistry Department, The University, Dundee DD1 4HN, Scotland

Acylals (8) are produced by the reaction of benzaldehyde with methyl diphenylphosphinite (4a) and carboxylic acids. One diastereoisomer of (8) is formed almost exclusively under mild conditions: the reasons for this are discussed. α -(α -Acetoxybenzyloxy)benzylidiphenylphosphine oxide (8a) is relatively inert to methanol. Analogues of (8), the 3-acyloxy-1,3-diphenylpropylphosphine oxides (9), have been synthesised and used in assignment of structure to the acylals (8).

MORE than 20 years have elapsed since Abramov first investigated the reaction of trialkyl phosphites with aldehydes, and showed that the thermal reaction affords α -alkoxyalkylphosphonates (1).² Since then, these aldehyde reactions have been studied by others,³ who have shown that, under milder conditions, intermediate 2:1 adducts can be isolated. These adducts have generally been found to be 1,4,2-dioxaphospholans, such as (2), formed from trimethyl phosphite and aliphatic aldehydes,⁴ or 1,3,2-dioxaphospholans, such as (3), formed by certain aromatic aldehydes.⁵ In general, however, aromatic aldehydes are unreactive to phosphorus(III) esters, and 1,3,2-dioxaphospholans have been isolated only from reactions of nitrobenzaldehydes^{5a} or pentafluorobenzaldehyde^{5b,c} with phosphites.

At the outset of our investigation of the reactions of

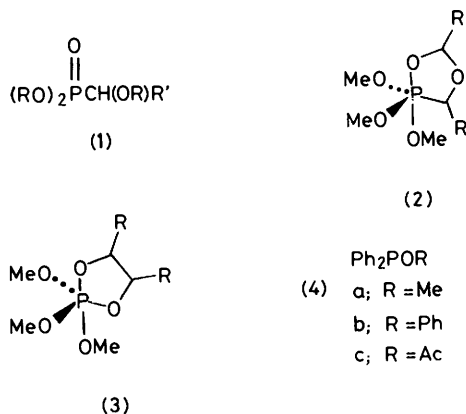
Thus benzaldehyde, *p*-chlorobenzaldehyde, and *p*-methoxybenzaldehyde do not react to any observable



SCHEME 1

extent with methyl diphenylphosphinite (4a) at ambient temperature, whereas *p*-nitrobenzaldehyde yields a mixture of diastereoisomeric 1,3,2-dioxaphospholans (5) (see Scheme 1).

We sought some means whereby the (presumed kinetic) inertness of the benzaldehyde-phosphinite ester system could be overcome. One obvious ploy was to incorporate an acidic species, in the hope that this might exert a catalytic influence on the addition of (4a) to the aldehydic carbonyl group. Accordingly, the effect of adding acetic acid was examined, using ¹H n.m.r. as a convenient probe. Addition of a few percent of acetic acid to a solution of (4a) and benzaldehyde did not appear to have the desired effect. However, in the presence of an equimolar amount of acetic acid benzaldehyde, methyl diphenylphosphinite, and the acetic acid were consumed steadily over 2 days at ambient temperature. The changes in the ¹H n.m.r. spectrum



diphenylphosphinite esters with simple aromatic aldehydes, we observed a pattern of reactivity analogous to that recorded by Ramirez⁵ for trimethyl phosphite.

¹ Part 8, J. A. Miller and D. Stewart, *J.C.S. Perkin I*, 1977, 1898.

² V. S. Abramov, *Doklady Akad. Nauk. S.S.S.R.*, 1954, **95**, 991 (*Chem. Abs.*, 1955, **49**, 6084).

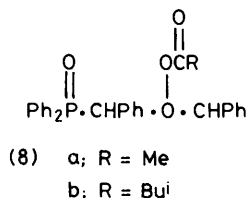
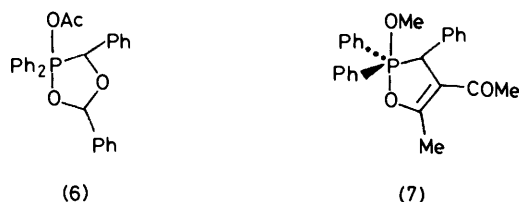
³ For leading reviews see (a) F. Ramirez, *Accounts Chem. Res.*, 1968, **1**, 168; (b) F. Ramirez, *Pure Appl. Chem.*, 1964, **9**, 337; (c) B. A. Arbusov and N. A. Polezhaeva, *Russ. Chem. Rev.*, 1974, **43**, 414; (d) I. V. Konvalova and A. N. Pudovik, *Russ. Chem. Rev.*, 1972, **41**, 411; (e) F. Ramirez, *Bull. Soc. chim. France*, 1970, 3492.

⁴ F. Ramirez, A. V. Patwardhan, and S. P. Heller, *J. Amer. Chem. Soc.*, 1964, **86**, 514.

⁵ (a) F. Ramirez, S. B. Bhatia, and C. P. Smith, *Tetrahedron*, 1967, **23**, 2067; (b) F. Ramirez, C. P. Smith, J. F. Pilot, and A. S. Gulati, *J. Org. Chem.*, 1968, **33**, 3787; (c) F. Ramirez, J. F. Pilot, C. P. Smith, S. B. Bhatia, and A. S. Gulati, *J. Org. Chem.*, 1969, **34**, 3385.

during this time suggested that the principal products were methanol and a 2:1:1 adduct of aldehyde, phosphinite, and acetic acid [δ 1.47 (3 H, s), 5.6 (1 H, d, J 11 Hz), and 6.9 (1 H, s)]. The adduct was isolated in 60% yield by precipitation and microanalytical figures were consistent with the molecular formula $C_{25}H_{25}O_4P$. A mass spectrum showed no molecular ion peak corresponding to this formula (M 456), but the fragment ions observed, *viz.* m/e 397 ($-\text{CH}_3\text{CO}_2$), 350 ($-\text{PhCHO}$), 308 ($-\text{PhCHO}$, $-\text{CH}_2\text{CO}$), 291 ($-\text{PhCHO}$, $-\text{CH}_3\text{CO}_2$), and 244 ($-\text{2PhCHO}$), are in good agreement with a structural formula in which are incorporated two aldehyde units, one $\text{Ph}_2\text{P}(\text{O})$ unit, and an acetate unit.

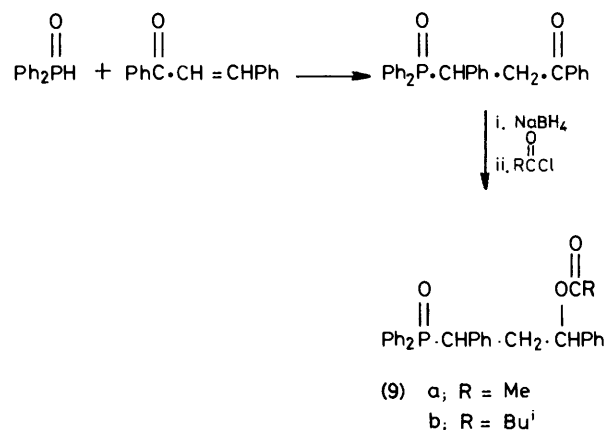
An i.r. spectrum of the adduct confirmed that an acetate carbonyl group was present, and was also suggestive of a phosphoryl group. On the other hand, the unusually low δ value for the acetate methyl in the ^1H n.m.r. spectrum was enigmatic. It seemed that such a shift might be explained if the adduct had a phosphorane structure (6), where the methyl protons could



be shielded by one or more of the three adjacent phenyl groups. One fairly good precedent has been noted in that the methoxy-protons in (7) resonate at rather high field (δ 2.63).⁶ The coupling constants $^3J_{\text{PH}}$ (for the C-5 proton) and $^4J_{\text{PH}}$ (for the acetyl protons) could conceivably ^{5c} be <1 Hz in (6).

However, the ^{31}P n.m.r. shift of the adduct (δ -26.9 p.p.m.) renders the phosphorane hypothesis untenable.⁷ We therefore considered other structures which were compatible with the above data; the oxide (8a) seemed an attractive possibility. Support for this structural assignment came from the $\{^1\text{H}\}^{13}\text{C}$ n.m.r. spectrum of the adduct, and by comparison of the ^{13}C n.m.r. data with those of one diastereoisomer of (9a), prepared from benzylideneacetophenone, as in Scheme 2. The methyl and carbonyl carbon atoms of (8a) give singlets at δ 20.26 and 170.0, respectively. Doublets due to the methine carbon atoms in the adduct appear at δ 81.75 (J_{PC} 88.4 Hz) and 97.80 (J_{PC} 12.2 Hz). The PC coupling constants are consistent with one-bond ($^1J_{\text{PC}_\alpha}$)

and three-bond ($^3J_{\text{PC}_\beta}$) interactions,⁸ and are similar to those found for (9a), *viz.* $^1J_{\text{PC}_\alpha}$ 70 Hz and $^3J_{\text{PC}_\beta}$ 15 Hz (one diastereoisomer). The ^1H chemical shifts of the

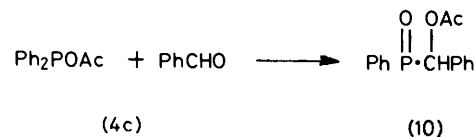


SCHEME 2

acetate methyls of the diastereoisomers of (9a), δ 1.93 and 1.8, are both quite low, but neither approaches the 'abnormal' shift of the methyl group in (8a).

We have found that in combination with (4a) and benzaldehyde, various other carboxylic acids function in a manner analogous to acetic acid. For example, isobutyric acid is transformed into (8b), the ^1H n.m.r. spectrum of which shows that the methine and methyl groups in the isopropyl moiety are shielded considerably. A similar, but smaller shielding effect is displayed by the methyl groups of one diastereoisomer of the methylene analogue (9b). We note the effect of $-\text{O}-$ in (8b) *versus* $-\text{CH}_2-$ in (9b) on the magnitude of the chemical shift non-equivalence, $\Delta\delta$,⁹ for the methyl groups: $\Delta\delta$ is significantly larger (0.115 p.p.m.) for (9b) than for (8b) (0.04 p.p.m.).

In contrast to the reaction of (4a) with benzaldehyde and acetic acid, phenyl diphenylphosphinite (4b) affords only a trace of (8a) under similar conditions. The major organophosphorus product afforded by a 2:1:1 mixture of aldehyde, (4b), and acetic acid was α -acetoxybenzylidenediphenylphosphine oxide (10), identical with an authentic sample prepared from acetoxydiphenylphosphine (4c) and benzaldehyde¹⁰ (see Scheme 3). If an



SCHEME 3

excess of aldehyde (*ca.* 6 mol. equiv.) is present in the initial reaction mixture, a significant quantity of (8a) is produced, though it is still a minor component of the product mixture.

The novel acylal (8a) appears to be stable in dry air,

⁸ L. D. Quin, M. D. Gordon, and S. O. Lee, *Org. Magnetic Resonance*, 1974, **6**, 503.

⁹ W. B. Jennings, *Chem. Rev.*, 1975, **75**, 307.

¹⁰ W. P. Savage and S. Trippett, *J. Chem. Soc. (C)*, 1966, 1842.

⁶ Ref. 3a, p. 172.

⁷ M. M. Crutchfield, C. H. Dungan, J. H. Letcher, V. Mark, and J. R. Van Wazer, *Topics Phosphorus Chem.*, 1967, **5**, 48; ref. 3d, p. 425.

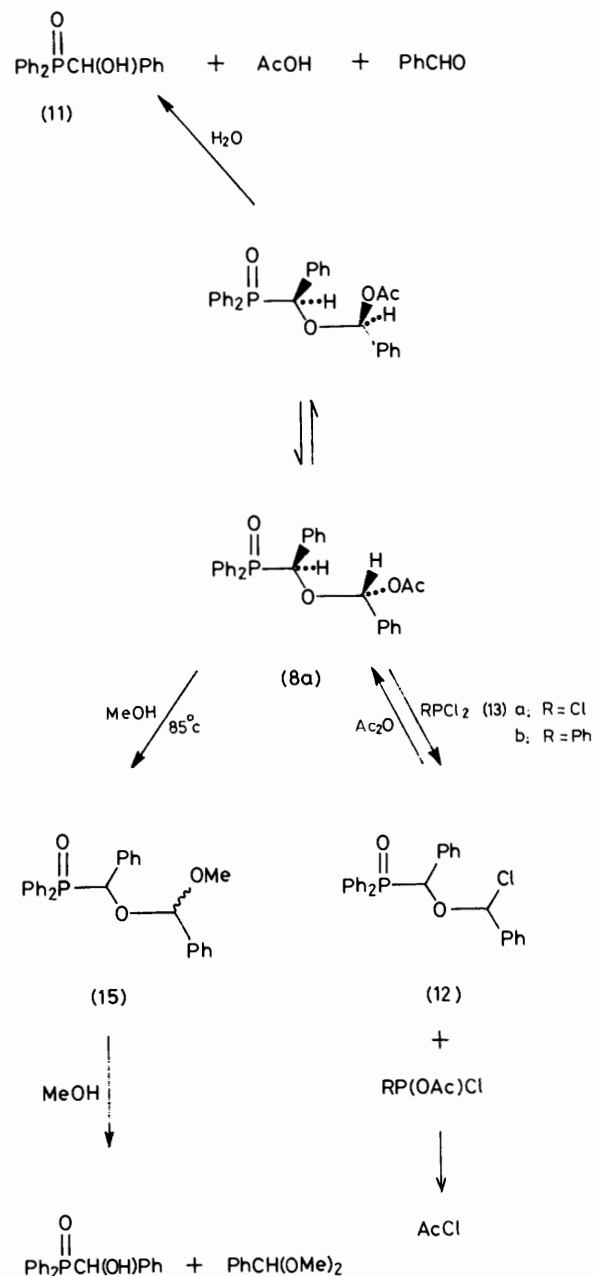
and can be recrystallized in an open flask, provided the solution (benzene plus a few percent of acetic acid to aid dissolution) is not warmed above *ca.* 30 °C. Lack of careful handling in this respect results in formation of α -hydroxybenzylidenediphenylphosphine oxide (11), benzaldehyde, and acetic acid.

On heating a dry solution of (8a) in deuteriochloroform in a sealed n.m.r. tube, ^1H n.m.r. spectral changes occurred which we tentatively ascribe to isomerization. Thus, after 9 h at 85 °C a spectrum indicated that more than half the original acetate had been consumed, and showed new absorptions at δ 1.95 (3 H, s), 5.75 (1 H, d, J 11.5 Hz), and 6.75 (1 H, s). It seems likely that these can be attributed to the diastereoisomer of (8a), though we have not been able to obtain a 'clean' sample of this material for full spectroscopic and analytical characterisation. The composition of the mixture was unaffected by further heating at 85 °C, or at a higher temperature (120 °C), and the system had apparently attained a state of dynamic equilibrium (see Scheme 4). Similarly constituted mixtures of the two acetates (8a) were produced in a reaction of (4a) with benzaldehyde in the presence of an excess of acetic acid (*ca.* 6.5 mol. equiv.), and in an experiment in which the α -chloro-ether (12) ¹¹ was treated with acetic anhydride.

The reverse of the latter process, exchange of chloride for acetate in (8a), is readily accomplished at room temperature using phosphorus trichloride (13a) or dichlorophenylphosphine (13b).¹² An ^1H n.m.r. study of this interconversion revealed several noteworthy features. Thus, phosphorus trichloride (13a) reacts faster than the dichlorophosphine (13b), and, moreover, spectral changes occur which are indicative of isomerization of (8a) (see above) under the reaction conditions. In spite of this, only one diastereoisomer of the α -chloro-ether product (12) [δ 6.05 (d, J 8.5 Hz) and 6.44 (s)] seems to be formed.¹¹ We also observed that the initially formed phosphorus(III) products are slowly transformed into acetyl chloride.

On the other hand, the stability of the acylal (8a) to methanol contrasts with the rapid reaction which occurs between methanol and α -methoxybenzyl acetate (14) at room temperature (Scheme 5). Even after several hours at 75 °C, a solution of (8a) in deuteriochloroform containing methanol (*ca.* 15% excess) had undergone little change in composition (^1H n.m.r.). After a few hours at 85 °C, new methoxy-resonances had begun to appear at δ 2.86 and 3.17. These were accompanied by signals due to acetic acid and isomerized acylal (see above), and the appearance of a group of low-intensity peaks between δ 5.25 and 6.0. Continued heating for 7 h led to complete loss of acylal (8a), and formation of benzaldehyde dimethyl acetal (*ca.* 15%), benzaldehyde (*ca.* 10%), and α -hydroxybenzylidenediphenylphosphine oxide (11). The methoxy-compounds responsible for the signals at δ 2.86 and 3.17 accounted for *ca.* 55% of the original acylal. The changes in the proportions of these

methoxy-signals throughout the heating operation indicated that the species responsible were decomposing



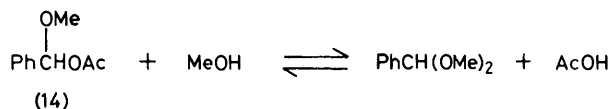
SCHEME 4

slowly under these conditions. Furthermore, the remainder of the aliphatic spectrum contained four methine signals (2 singlets: δ 5.25, 5.40; and 2 doublets: δ 5.28, 5.88) and these, together with the high-field methoxy-signals, are tentatively assigned to the diastereoisomers of the mixed acetal (15) (see Scheme 4).

¹² M. B. Gazizov, D. B. Sultanova, A. I. Razumov, L. P. Ostanina, T. V. Zykova, and E. I. Savee'eva, *J. Gen. Chem., U.S.S.R.*, 1974, **44**, 1235; M. B. Gazizov, D. B. Sultanova, A. I. Razumov, T. V. Zykova, N. A. Anoshina, and R. A. Salukhtinov, *ibid.*, 1975, **45**, 1670.

¹¹ N. J. De'ath, J. A. Miller, and M. J. Nunn, *Tetrahedron Letters*, 1973, 5191.

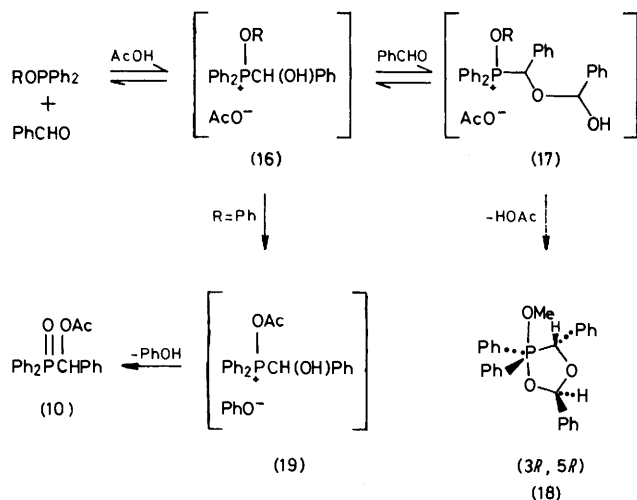
Further support for the suggestions outlined in Scheme 4 comes from an experiment in which the course of the methanolysis in hexadeuteriobenzene was followed using ^1H n.m.r. In this solvent the methyl resonances of methanol and benzaldehyde dimethyl acetal are well



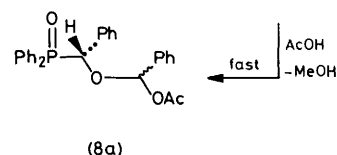
SCHEME 5

separated, and it was clear that the latter was not produced until considerable amounts of the 'high-field' methoxy-products (15) had accumulated.

To return to the reaction in which the acylal (8a) is formed, it is worth considering what light is shed by our results on the mechanism of this process. By making the assumption that the tervalent phosphorus functions as a nucleophile in its initial interaction with benzaldehyde, we can envisage the formation of (8a) in the manner shown in Scheme 6, *i.e.* sequential formation of intermediates (16) and (17) by successive addition of two aldehyde molecules to (4), in the presence of acetic acid, followed by transformation of the latter 2 : 1 : 1 adduct into (8a), probably *via* the 1,4,2-dioxaphospholan (18).



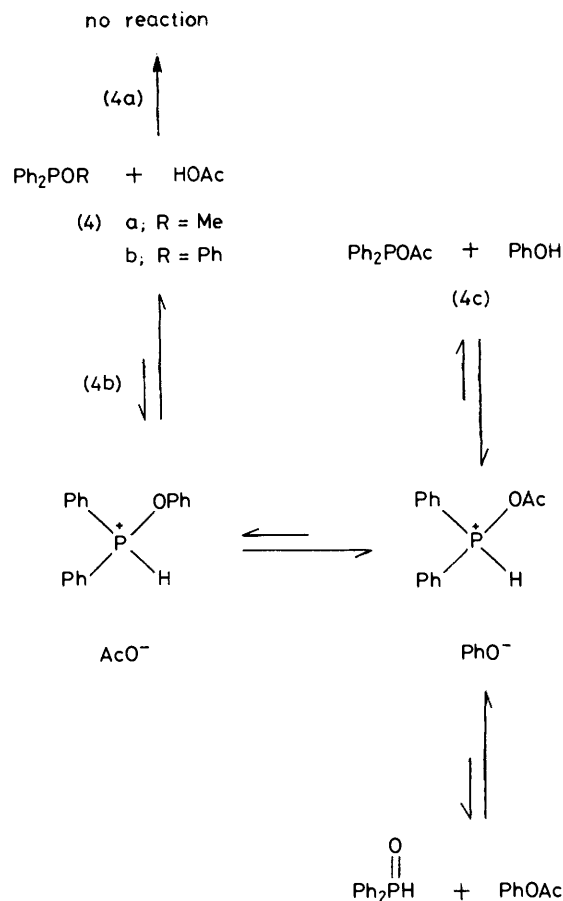
SCHEME 6



SCHEME 6

The fact that acetoxydiphenylphosphine (4c) and benzaldehyde yield α -acetoxybenzylidiphenylphosphine oxide (10) relatively rapidly, in the presence or in the absence of acetic acid, points to the propensity of the 1 : 1 adduct (19) to undergo transacetylation. This, in turn, implies that in the reaction of (4a), replacement of

methoxy on phosphorus by acetoxy is not appreciable, either in the reactant, or at the stage of the 1 : 1 adduct (16; R = Me), since no α -acetoxybenzylidiphenylphosphine oxide (10) was ever detected in the final product mixture. Conversely, the predominance of (10) in the product from reaction of phenyl diphenylphosphinite (4b) signifies that, in this case, exchange at phosphorus is a kinetically favourable process, leading to (10) *via* the acetoxyphosphonium intermediate (19). An indication of the relative ease¹³ with which *P*-OMe and *P*-OPh groups are replaced by acetate is provided by the results of a simple experiment, in which (4a) and



SCHEME 7

(4b) were treated separately with acetic acid. Whereas the methyl ester (4a) was apparently unchanged after 1 day at 33 °C, a few per cent of phenyl acetate was formed from (4b) in the same period (Scheme 7). The fact that some acylal (8a) is produced in minor amounts in reactions of (4b) with benzaldehyde, and that the proportion of (8a) formed is increased significantly by employing an excess of aldehyde at the start, is in line with what one would predict, *a priori*, from Scheme 6.

¹³ T. Kh. Gazizov, Y. Y. Efremov, R. Z. Musin, A. P. Pashinkin, V. A. Kharlamov, and A. N. Pudovik, *J. Gen. Chem., U.S.S.R.*, 1974, **44**, 1827; A. N. Pudovik, V. E. Belskii, T. Kh. Gazizov, A. P. Pashinkin, and M. F. Efremova, *ibid.*, 1975, **45**, 2582.

Thus we have no evidence that an acetoxyphosphonium species lies on the route to (8a). The same can be said of pathways involving possible acetolysis of a mixed acetal, such as (15), in view of the kinetic stability of (15) towards acetic acid. Such considerations lead us to suggest that (18) is a likely intermediate in the formation of (8a). Not only is there good analogy for (18) in the 1,4,2-dioxaphospholans described elsewhere,^{4,5} but also the proposition that the oxyphosphorane (18) is an essential intermediate in the formation of (8a) provides a neat rationalization of two characteristics of the reaction. First, it explains why two molecules of benzaldehyde, and not more than two, become implicated in the product. Secondly, provided that an excess of acetic acid is not present, the acylal formed from (4a) is predominantly one diastereoisomer (*i.e.* ca. 85% or more). Stereoselectivity of this type, albeit of a lesser degree, has been noted previously, in the formation of 1,3,2-dioxaphospholans,¹⁴ and of 1,4,2-dioxaphospholans^{4,5} from aldehydes. Although the origins of this selectivity are by no means established, it is possible that one isomer of 2-methoxy-2,2-diphenyl-1,4,2-dioxaphospholan (18) could be formed with greater selectivity than observed^{4,5} with other phosphorus(III) esters. Dreiding models of the phosphorane (18) indicate that the (3*R*,5*R*)-diastereoisomer is likely to be significantly less congested than the other diastereoisomer, and that the presence of four phenyl groups might enhance, relative to previous cases, the energy difference between the diastereoisomers. Finally, it seems fairly certain that the predominant diastereoisomer of (8a) produced in the methyl phosphinite reaction is the 'kinetic product,' the 'thermodynamic product' being obtained by equilibration under different conditions, such as the use of higher temperature, or increased acidity.

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 137 spectrometer. N.m.r. spectra for nuclei were recorded as follows: ¹H with a Perkin-Elmer R-10 spectrometer operating at 60 MHz (Me₄Si as internal standard); ³¹P with a Bruker spectrospin HX90 spectrometer operating at 24.3 MHz [positive shifts upfield from H₃PO₄ (85%)]; ¹³C spectra with a JEOL PS-100 spectrometer.

Phosphorus trichloride, dichloro(phenyl)phosphine, and diphenylphosphinite esters were all redistilled in dry apparatus and stored at 0 °C under nitrogen. Benzaldehydes were either redistilled, or recrystallized and dried, before use. Acetic acid and isobutyric acid were redistilled. Solvents were all dried and redistilled.

Reactions of Methyl Diphenylphosphinite (4a) with Aromatic Aldehydes.—(a) *p*-Nitrobenzaldehyde. A mixture of methyl diphenylphosphinite (2.16 g, 10⁻² mol) and *p*-nitrobenzaldehyde (3.10 g, 2 × 10⁻² mol) in dry chloroform (15 ml) was flushed with dry nitrogen. The aldehyde dissolved fairly rapidly after the ester was added. The ¹H n.m.r. doublet due to the starting ester (δ 3.62, *J* 14.0 Hz) was slowly replaced by other doublets of comparable intensity at higher field [δ 3.38 (*J* 11.0 Hz) and 3.2 (*J* 11.0 Hz)]. Simultaneously the aldehyde CHO absorption diminished, and absorptions appeared at δ 5.35 (d, *J*

12 Hz) and 4.68 (s). Repeating this reaction in deuteriated acetonitrile (in which the proportions of the products were different) showed that the δ 3.38 and 4.68 absorptions (integral 3 : 2) belonged to one isomer of the 1,3,2-dioxaphospholan (5), while the others belonged to the other isomer. It was not possible to separate these by fractional crystallization, although the crude mixture was solid. The mixture showed no i.r. absorption in the C=O region. The mixture showed ³¹P δ +28 p.p.m.

(b) *Other aldehydes.* Similar solutions in deuteriochloroform were made up in turn with benzaldehyde, *p*-chlorobenzaldehyde, and *p*-methoxybenzaldehyde in place of *p*-nitrobenzaldehyde. ¹H N.m.r. spectra showed that no reaction had occurred after 5 days at room temperature. In the case of the benzaldehyde-methyl diphenylphosphinite solution, no reaction was observed after heating at 100 °C for 10 h. Addition of a trace of acetic acid (10⁻³ mol. equiv.), followed 18 h at room temperature, made no difference to the spectrum.

Reactions of Benzaldehyde with Methyl Diphenylphosphinite (4a) in the Presence of at Least Molar Equivalent Quantities of Carboxylic Acids.—(a) *One equiv. of acetic acid.* Methyl diphenylphosphinite (0.216 g, 10⁻³ mol), benzaldehyde (0.212 g, 2 × 10⁻³ mol), and acetic acid (0.060 g, 10⁻³ mol) were dissolved in deuteriochloroform (3 ml) and the mixture was stirred under nitrogen at room temperature for 48 h. During this time both the ester OMe and aldehyde CHO ¹H n.m.r. absorptions fell to about 10% of their original strength. New absorptions appeared at δ 6.9 (s), 5.95 (d, *J* 10 Hz), 5.6 (d, *J* 11 Hz), 5.5 (m), 5.32 (s), 3.4 (two s), 3.15 (s), 2.85 (s), 1.95 (s), 1.78 (s), and 1.47 (s).

When this reaction was repeated on a larger scale (2 × 10⁻² mol) (benzaldehyde 5.3 g, 5 × 10⁻² mol), using 90% petrol (b.p. 40–60 °C) in benzene (50 ml total) as solvent, a white precipitate (4.2 g) formed after 20 h stirring at room temperature. This was filtered off and washed with petrol. A further precipitate (1.0 g) was obtained after 1 day. These precipitates were identical, and were recrystallized from benzene-petrol to which a small portion of acetic acid had been added to give one diastereoisomer of α-(α-acetoxybenzyloxy)benzylidiphenylphosphine oxide (8a), m.p. 145–147 °C; *v*_{max.} (Nujol) 1738 (C=O), 1240, 1187 (P=O), 1119, 1063, 998, 963, 702, and 693 cm⁻¹; δ_H 8.0–7.0 (20 H, m), 6.9 (1 H, s), 5.6 (1 H, d, *J* 11 Hz), and 1.47 (3 H, s); δ_P (CDCl₃) -26.9 p.p.m.; {¹H} ¹³C δ 20.26 (s, Me), 81.75 (d, ¹*J*_{CP} 88.4 Hz), 97.80 (d, ³*J*_{CP} 12.2 Hz), and 170.0 (s, C=O); *m/e* 397, 350, 308, 291, 244, 202, 201, 183, 167, 155, 124, 106, and 105 (Found: C, 73.5; H, 5.65; P, 6.75. C₂₈H₂₅O₄P requires C, 73.65; H, 5.5; P, 6.8%).

(b) *Excess of acetic acid.* Methyl diphenylphosphinite (0.164 g, 0.76 × 10⁻³ mol), benzaldehyde (0.161 g, 1.52 × 10⁻³ mol), and acetic acid (0.3 g, 5 × 10⁻² mol) were dissolved in deuteriochloroform (2 ml); after 15 min ¹H n.m.r. indicated that most of the ester (>95%) had been consumed. The spectrum showed absorptions at δ 6.94 (s), 5.89 (d, *J* 11 Hz), and 1.47, which gave relative integrals 1 : 1 : 3 expected for one diastereoisomer of the acylal (8a) (isolated above), as well as other bands at δ 6.79 (s), 6.05 (d, *J* 9.5 Hz), and 1.70 (s). The latter group of signals was stronger than that due to (8a). Traces of methyl acetate [δ 3.58 (s)], and α-hydroxybenzylidiphenylphosphine oxide (11) [δ 5.8 (d, *J* 4 Hz)] were also observed, in addition to

¹⁴ F. Ramirez, A. S. Gulati, and C. P. Smith, *J. Org. Chem.*, 1968, **33**, 13.

methanol [δ 3.4 (s)]. Attempts to separate the diastereoisomers of the adduct (8a) were not successful.

(c) *One equiv. of isobutyric acid.* Methyl diphenylphosphinite (0.195 g, 0.84×10^{-3} mol), benzaldehyde (0.192 g, 1.81×10^{-3} mol), and isobutyric acid (0.08 g, 0.91×10^{-3} mol) were dissolved in deuteriochloroform (2 ml) under nitrogen. After 16 h at room temperature the system appeared to have reached equilibrium, in that the ^1H n.m.r. absorptions due to starting materials had ceased to diminish, and new absorptions at δ 6.95 (s), 5.85 (d, J 10.5), 2.05 (m), 0.75 (t, J ca. 7 Hz) were no longer increasing in intensity. The new absorptions appeared in the ratio 1 : 1 : 1 : 6, and accounted for about 40% of the starting materials. Repeated attempts to isolate a pure adduct from this system were unsuccessful.

Reactions of Phenyl Diphenylphosphinite with Benzaldehyde.—Mixtures of phenyl diphenylphosphinite (0.278 g, 10^{-3} mol) and benzaldehyde (0.212 g, 2×10^{-3} mol) were dissolved in deuteriochloroform (2 ml) under nitrogen and used for the following experiments.

(a) The mixture was heated gradually to 120 °C, but there was no evidence (^1H n.m.r.) of any reaction.

(b) To the mixture was added acetic acid (0.060 g, 10^{-3} mol) and the solution was maintained at 30 °C for 12 days. Evaporation yielded a clear oil, which, on trituration with petrol (b.p. 40–60 °C) to which a little ether had been added, yielded a solid. Recrystallization [benzene–petrol (b.p. 40–60 °C)] gave α -acetoxybenzylidiphenylphosphine oxide (10) (52%), m.p. 169–171 °C (lit.,¹⁰ 171–172 °C); ν_{max} . (Nujol) 1 747, 1 223, 1 200, and 1 190 cm^{-1} . An ^1H n.m.r. spectrum of the crude mixture revealed other products, shown by signal augmentation to be the acylal (8a) (<5%) and phenyl acetate (20%).

(c) To the mixture was added acetic acid (0.060 g, 10^{-3} mol) and a further quantity of benzaldehyde (0.530 g, 5×10^{-3} mol). After 3 days at room temperature ^1H n.m.r. revealed the same components as described above. By signal augmentation, these were identified as α -acetoxybenzylidiphenylphosphine oxide (10) (45%), the acylal (8a) (10%), phenyl acetate (7%), and unchanged acetic acid (38%).

Reactions of the Acylal (8a).—(a) *Heat.* A solution of the acylal (8a) (0.2 g, 4.38×10^{-4} mol) in deuteriochloroform (0.5 ml) containing *t*-butylbenzene was warmed gradually to 80 °C. At temperatures above this, the ^1H n.m.r. signals due to starting material (see above) diminished gradually, and were replaced by stronger signals at δ 6.75 (s), 5.75 (d, J 11.5 Hz), and 1.95 (s). These were in the ratio 1 : 1 : 3. Once the new signals had reached an intensity ca. 50% greater than those due to the starting acylal, no further change was observed, even after several hours in the range 85–120 °C. This spectrum was almost identical with that of the mixture of diastereoisomers of (8a), produced from benzaldehyde in the presence of an excess of acetic acid (see above). The mixture of diastereoisomers showed only one ^{31}P n.m.r. absorption, at the same shift as the starting material.

(b) *With phosphorus(III) chlorides.* A solution of the acylal (8a) (0.2 g, 4.38×10^{-4} mol) in deuteriochloroform (0.5 ml) was treated with phosphorus trichloride (0.06 g, 4.4×10^{-4} mol). After 15 min the ^1H n.m.r. signals due to (8a) had been reduced to 15% (relative to *t*-butylbenzene) of their original strength. New absorptions at

δ 6.44 (1 H, s) and 6.05 (1 H, d, J 85 Hz) overlapped exactly with those from a pure sample of one diastereoisomer of the ether (12). The ^1H n.m.r. of the mixture also showed peaks close to δ 2.0; these slowly diminished and acetyl chloride (δ 2.58) was formed.

Similar results were obtained when dichloro(phenyl)phosphine (13b) was used instead of phosphorus trichloride, but the reaction was noticeably slower. In both reactions conversion into α -chloro-ether was slower than isomerisation of the acylal (8a).

(c) *With methanol.* To a solution of the acylal (8a) (0.2 g, 4.38×10^{-4} mol) in deuteriochloroform (0.5 ml) was added dry methanol (0.0151 g, 5.06×10^{-4} mol). The mixture was unchanged after several hours at any temperature below 75 °C. At 85 °C gradual isomerisation of the acylal (8a) was observed by ^1H n.m.r. After 10 h at this temperature the diastereoisomeric mixture of acylals had largely been converted into acetic acid, and most of the methanol had been consumed. A ^1H n.m.r. spectrum of the mixture showed signals at δ 5.88 (d, J 10.5 Hz), 5.58 (d, J 6.5 Hz), 5.28 (d, J 10.2 Hz), 5.43 (s), 5.40 (s), 5.25 (s), 3.33 (s), 3.17 (s), and 2.86 (s), as well as absorptions in the 8.0–7.0 region.

Evaporation resulted in precipitation of α -hydroxybenzylidiphenylphosphine oxide (11), m.p. 176–178 °C (lit.,¹⁵ 178–179.5 °C), whose i.r. spectrum was identical with that of an authentic sample. Signal augmentation studies showed that this oxide was responsible for the δ 5.58 (d) absorption, and that small amounts of benzaldehyde dimethyl acetal were responsible for the singlets at δ 5.43 and 3.33 (relative intensity 1 : 6).

When this reaction was repeated in hexadeuteriobenzene (0.5 ml) at 85 °C, the reaction was slower, and it was clear that the absorptions due to the oxide (11) and benzaldehyde dimethyl acetal only appeared after the other absorptions. Thus after 2 h at 85 °C singlet methoxy-absorptions appeared at δ 3.02 and 2.76, and their combined integral was the same as that of acetic acid (δ 1.88). After 8 h at 85 °C, benzaldehyde dimethyl acetal (δ 3.17) began to form. The mixed acetal with δ 3.02, appeared more rapidly, but, as heating continued, the more stable diastereoisomer predominated, and larger amounts of α -hydroxybenzylidiphenylphosphine oxide (11) and benzaldehyde dimethyl acetal began to accumulate. It was not possible to separate the diastereoisomers of the methyl acetals (15).

(d) *With water.* The acylal (8a) (0.456 g, 10^{-3} mol) was dissolved in dioxan to which water had been added. Warming the solution in a nitrogen atmosphere produced acetic acid and benzaldehyde, in equal amounts. Evaporation of volatile material and trituration of the residue with petrol (b.p. 40–60 °C) yielded α -hydroxybenzylidiphenylphosphine oxide (11) (0.276 g, 90%).

(α -Phenacylbenzyl)diphenylphosphine Oxide.—This was prepared by an improved version of an earlier procedure.¹⁶ To a solution of chlorodiphenylphosphine (13.8 g, 6.27×10^{-2} mol) in tetrahydrofuran–ether (1 : 1; 40 ml) was added water (1.12 g, 6.25×10^{-2} mol) in tetrahydrofuran (10 ml), while the mixture was stirred vigorously and cooled in a water-bath. After 30 min a solution of benzylideneacetophenone (12.0 g, 5.76×10^{-2} mol) in ether (30 ml) was added rapidly, and the mixture stirred under nitrogen at room temperature for 24 h. The precipitate was filtered off and dissolved in methylene chloride and the solution

¹⁵ R. C. Miller, C. D. Miller, W. Rogers, and L. A. Hamilton, *J. Amer. Chem. Soc.*, 1957, **79**, 424.

¹⁶ J. A. Miller, G. M. Stevenson, and B. C. Williams, *J. Chem. Soc. (C)*, 1971, 2714.

washed with dilute aqueous sodium hydrogen carbonate, then water. After drying, the solvent was removed and the residue recrystallized from toluene to give (α -phenacylbenzyl)diphenylphosphine oxide (14.65 g, 62%), m.p. 234—236 °C (lit.,¹⁷ 235—237 °C).

(3-Acetoxy-1,3-diphenylpropyl)diphenylphosphine Oxide (9a).—(α -Phenacylbenzyl)diphenylphosphine oxide (5.5 g, 1.34×10^{-2} mol) was dissolved in warm ethanol (140 ml at 60 °C). Sodium borohydride (1.0 g) was then added in several portions and the mixture stirred for 2.5 h, after which the solution was clear. The mixture was poured into dilute hydrochloric acid and ice, and the resultant precipitate filtered off, then washed with water. After drying to constant weight (5.5 g), the powdery product showed ν_{\max} (Nujol) 3 340br, 1 440, 1 152, 743, 723, and 700 cm^{-1} , and was taken to be the desired alcohol.

A sample of the alcohol (1.0 g, 2.42×10^{-3} mol) was suspended and partially dissolved in chloroform (15 ml). Acetyl chloride (0.4 g, 5.1×10^{-3} mol) was then added and the mixture stirred overnight, after which a clear solution had been formed. The solution was dried (K_2CO_3) and evaporated to leave an oily solid (1.22 g). A ^1H n.m.r. spectrum revealed two strong singlets (δ 1.93 and 1.79), taken to be due to the diastereoisomers (9a), present in the ratio 55 : 45.

The diastereoisomers were separated by crystallization from ether containing a little petrol (b.p. 40—60 °C). The insoluble material (0.7 g) consisted largely of the 'low-field' acetate (δ 1.93), and this *diastereoisomer* was purified by further recrystallization from chloroform-ether; m.p. 185—188 °C; ν_{\max} (Nujol) 1 752, 1 227, 1 180, and 1 120 cm^{-1} ; δ_{H} 8.2—7.0 (20 H, m), 5.6 (1 H, m), 3.7 (1 H, m), 2.8—2.3 (2 H, m), and 1.93 (3 H, s); $\{^1\text{H}\}^{13}\text{C}$ δ 169.6 (s, C=O), 73.5 (d, $^3J_{\text{CP}}$ 15.3 Hz), 43.2 (d, $^1J_{\text{CP}}$ 70 Hz), 36.3 (d), and 2.07 (s, Me) (Found: C, 76.7; H, 6.1. $\text{C}_{29}\text{H}_{27}\text{O}_3\text{P}$ requires C, 76.65; H, 6.0%).

The mother liquor from the initial crystallization yielded a solid (0.45 g) which was mainly the 'high-field' (δ 1.79) acetate. This was recrystallized from ether-petrol (b.p. 40—60 °C) to give the second *diastereoisomer* (9a), m.p. 174—177 °C; ν_{\max} (Nujol) 1 734, 1 245, 1 173, and 1 120 cm^{-1} ; δ_{H} 8.0—7.1 (20 H, m), 5.55 (1 H, m), 3.2—2.3 (3 H, m), and 1.80 (3 H, s) (Found: C, 76.4; H, 5.95; P, 6.65. $\text{C}_{29}\text{H}_{27}\text{O}_3\text{P}$ requires C, 76.65; H, 6.0; P, 6.8%).

(3-Isobutyryloxy-1,3-diphenylpropyl)diphenylphosphine Oxide (9b).—(α -Phenacylbenzyl)diphenylphosphine oxide was reduced as above and the alcohol product (1.1 g, 2.66×10^{-3} mol) treated with isobutyryl chloride (1.06 g, 10^{-2} mol) in chloroform at room temperature for 30 h. Work-up as above yielded an oil (1.4 g), the ^1H n.m.r. spectrum of which showed two dd signals (δ 1.15 and 1.01) at high field. The presumed diastereoisomers were separated by fractional crystallization from ether-chloroform, and the more soluble crystallized twice from petrol (b.p. 40—60 °C)-toluene; m.p. 183—184 °C; ν_{\max} (Nujol) 1 724, 1 200, 1 170, and 1 160 cm^{-1} ; δ_{H} 7.8—7.0 (20 H, m), 5.5 (1 H, m), 3.2—2.2 (4 H, m), 1.00 (6 H, dd, $^2J_{\text{PH}}$ 7.0 and 7.2 Hz) (Found: C, 77.8; H, 6.4. $\text{C}_{31}\text{H}_{31}\text{O}_3\text{P}$ requires C, 77.15; H, 6.5%).

Conversion of the α -Chloro-ether (12) into the Acylal (8a).—

α -Chlorobenzyl α -(diphenylphosphinoyl)benzyl ether (12) was made from benzaldehyde and chlorodiphenylphosphine (2.2 g, 10^{-2} mol).¹¹ To a solution of (12) (0.43 g, 10^{-2} mol) in deuteriochloroform under nitrogen was added acetic anhydride (0.51 g, 5×10^{-3} mol), and the mixture was kept at 33 °C. The ^1H n.m.r. spectrum revealed the slow but steady loss of the signals due to the ether (12) over 24 h. A mixture of the diastereoisomers (8a) was formed, as shown by signal augmentation with the mixture of diastereoisomers (8a) formed from benzaldehyde in the presence of an excess of acetic acid. The proportions of the isomers were also very similar, in that the acylal with the high-field acetate signal (δ 1.70) predominated (*ca.* 2 : 1). Acetyl chloride was also formed, and integration of the δ 2.6 signal showed that it was produced in amount equal to that of the diastereoisomers (taken together).

Reaction of Acetic Acid with Diphenylphosphinite Esters.—An equimolar mixture of the diphenylphosphinite (10^{-3} mol) and acetic acid in deuteriochloroform (0.5 ml) was sealed under nitrogen at 20 °C and examined periodically by ^1H n.m.r. (t-butylbenzene as internal integral standard).

With phenyl diphenylphosphinite (4b), there was scarcely any change in the intensity of the signal due to acetic acid (δ 1.99) after 10 h. After 2 days, a trace of acetoxydiphenylphosphine (s, δ 2.12) was observed (<3%). When an excess (5 mol. equiv.) of acetic acid was added, and the mixture set aside for 3 days, diphenylphosphine oxide (d, δ 8.23) and phenyl acetate (s, δ 2.2) were each detected in small amounts (*ca.* 10%).

With methyl diphenylphosphinite (4a), no spectral changes were observed after 2 days at room temperature; even in the presence of an excess of acetic acid (4a) was unchanged.

Preparation of α -Methoxybenzyl Acetate (14) and its Reaction with Methanol.—Benzaldehyde dimethyl acetal was converted into methyl α -chlorobenzyl ether with acetyl chloride and thionyl chloride,¹⁸ and this ether was converted into α -methoxybenzyl acetate (14), b.p. 109—110 °C at 13 mmHg (lit.,¹⁹ 115—117 °C at 15 mmHg) using sodium acetate. The ^1H n.m.r. spectrum of the acetate showed δ 8.0—7.3 (5 H, m), 6.80 (1 H, s), 3.57 (3 H, s), and 2.14 (3 H, s). Addition of dry methanol (1 mol. equiv.) resulted in extremely rapid conversion (<1 min) into benzaldehyde dimethyl acetal (>95%). From a study of this equilibrium, and of the reaction of acetic acid (in excess) with the acetal, it was clear that K_{eq} for the equilibrium (in Scheme 5) was *ca.* 250. There was no indication that the acetate (14) was in equilibrium with benzaldehyde and methyl acetate under any of the above conditions.

We thank Dr. C. Brown (University of Kent) and Dr. R. K. Mackie (University of St. Andrews) for ^{13}C n.m.r. spectra and mass spectra, respectively.

[7/693 Received, 25th April, 1977]

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