The Chemistry of Heteroarylphosphorus Compounds. Part IV.[1] The Effect of Substituents at Phosphorus on the Fate of Phosphobetaines in Protic Solvents. Studies of the Mechanism of the Wittig Reaction

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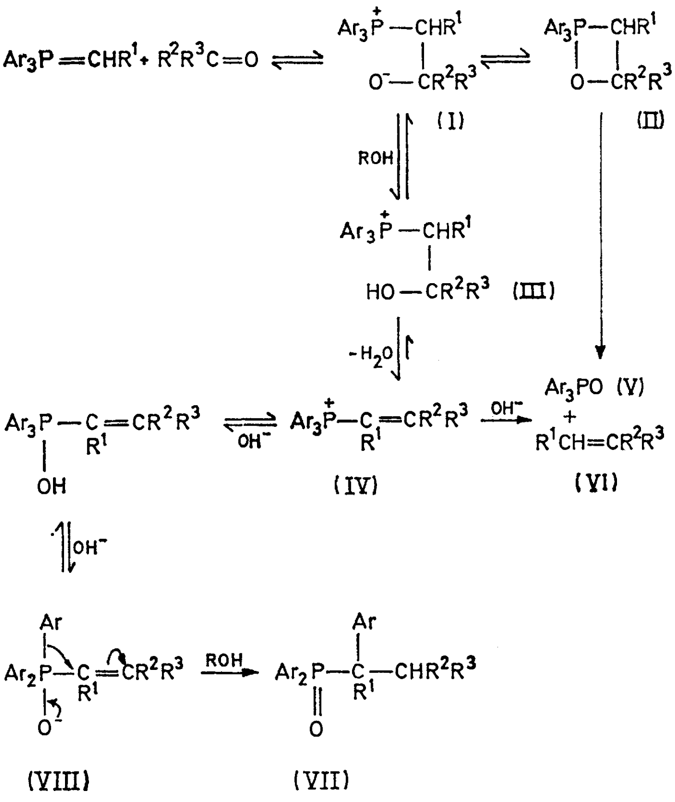
In order to investigate the effects of strongly electron-withdrawing substituents at phosphorus on the preferred mechanistic course of the Wittig reaction in protic solvents, a study has been made of the reactions of a series of phosphonium salts bearing 2-furyl substituents, with benzaldehyde, in alcoholic alkoxide media. It is shown that the presence of the electron-withdrawing 2-furyl substituent at phosphorus strongly favours intramolecular collapse of a cyclic oxaphosphetan intermediate leading to the ' normal ' Wittig products. Aryl-migration rearrangement products, derived from vinylphosphonium intermediates, are not observed in the reaction of methylphosphonium salts bearing 2-furyl substituents, in contrast to those of methylphosphonium salts bearing phenyl substituents. The results demonstrate that the preferred course of the reactions between phosphorus ylides and benzaldehyde in protic solvents is also dependent on the nature of the substituents at phosphorus.

SCHWEIZER *et al.*[2] have recently suggested an alternative mechanism to that of Wittig and Schollkopf[3,4] for the formation of olefins from phosphoranes and carbonyl reagents in alcoholic (protic) media. In such solvents, it was suggested that the intermediate betaine (I) is protonated [thereby preventing formation of the cyclic oxaphosphetan (II)] to give the β-hydroxyethylphosphonium salt (III). The latter eliminates water to form the vinylphosphonium salt (IV); for this to occur, there must be a proton α to the phosphonium group in (III), and additionally, one of the substituents, R^1, R^2, or R^3, must be capable of conjugating with the double bond in (IV). The vinylphosphonium salt then undergoes alkaline hydrolysis, on reaction with hydroxide ion derived from the water eliminated in the previous step, with loss of the vinyl group, to form the ' normal ' Wittig products (V) and (VI).

The intermediacy of a vinylphosphonium salt has also been suggested by Rakshys and McKinley[5] in order to account for a number of unexpected products in the reaction of 2-hydroxyalkyltriphenylphosphonium salts with base in protic solvents.

In an investigation of the generality of the Schweizer mechanism, Trippett *et al.*[6] studied the steric course of the Wittig reaction between optically active benzylethylmethylphenylphosphonium iodide and benzaldehyde in ethanolic sodium ethoxide solution. It was shown that the reaction occurred with retention of configuration at phosphorus, a result consistent with collapse of the cyclic oxaphosphetan (II) and not with the involvement of a vinylphosphonium intermediate, whose hydrolysis would have been expected to occur with inversion of configuration. Trippett *et al.* suggested that routes *via* oxaphosphetans (II) and vinylphosphonium salts (IV) are competitive, the preferred course depending particularly on the nature of the substituent on the carbon α to the phosphorus.

A number of related reactions which result in migration of an aryl group from phosphorus to carbon have also recently been shown to involve vinylphosphonium intermediates. While benzyltriphenylphosphonium halides give high yields of stilbenes in Wittig olefin syntheses with aromatic aldehydes in alkoxide media, methyltriarylphosphonium salts give only poor yields of olefins under the same conditions. Thus the major product of the reaction between methyltriphenylphosphonium iodide and benzaldehyde in ethanolic



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[1] Part III, D. W. Allen and B. G. Hutley, *J.C.S. Perkin II*, 1972, 67.

[2] E. E. Schweizer, D. M. Crouse, T. Minami, and A. T. Wehman, *Chem. Comm.*, 1971, 1000.

[3] G. Wittig and U. Schollkopf, *Chem. Ber.*, 1954, **87**, 1318.

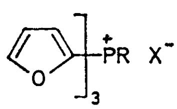
[4] A. Maerker, *Organic Reactions*, 1965, **14**, 270; A. W. Johnson, ' Ylid Chemistry,' Academic Press, New York, 1966.

[5] J. W. Rakshys and S. V. McKinley, *Chem. Comm.*, 1971, 1336.

[6] D. J. H. Smith and S. Trippett, *Chem. Comm.*, 1972, 191.

sodium ethoxide is the rearrangement product 1,2-diphenylethyldiphenylphosphine oxide (VII; Ar = Ph, $R^1 = R^2 = H$, $R^3 = Ph$). In addition, it has been shown that in the reactions of the iodides $MePh_2P^+$-C_6H_4X I^- with benzaldehyde in ethanolic sodium ethoxide, and in the reactions of the phosphines Ph_2-PC_6H_4X with styrene oxide in ethanol (which also result primarily in rearrangement products), the order of migration is *m*-chlorophenyl > phenyl > *p*-methoxyphenyl, that group migrating which is the more stable as a carbanion.[7] The course of these reactions, which involve 1,2-aryl migration from phosphorus to carbon, has recently been studied in depth and shown to involve the formation of an equilibrium mixture of a betaine (I), a hydroxyethylphosphonium salt (III), a vinylphosphonium salt (IV), and the corresponding pentacovalent oxyphosphorane (VIII).

Little is known of the influence of other substituents at phosphorus on the preferred course of the Wittig reaction. In our previous work on heteroarylphosphonium salts[9] we have shown that a 2-furyl substituent exerts a marked electron-withdrawing effect at phosphorus, and that the 2-furyl carbanion would appear to be significantly more stable than the benzyl carbanion, which in turn is more stable than the phenyl carbanion. Thus alkyltri-(2-furyl)phosphonium salts (IX; R = Me or $PhCH_2$) undergo alkaline hydrolysis some 10^{10} times faster than their phenyl analogues; furthermore, a 2-furyl group is cleaved from phosphorus more readily than is a benzyl group. In order to investigate the effects of electron-withdrawing substituents at phosphorus on the preferred course of the Wittig reaction in protic solvents, we have studied the reactions of a series of phosphonium salts bearing 2-furyl substituents, with benzaldehyde in alcoholic alkoxide media.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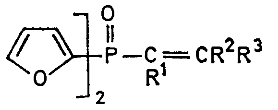
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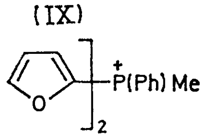
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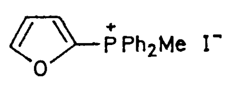
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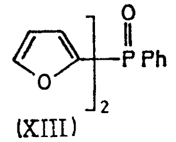
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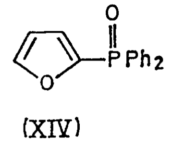
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It was considered that if the alternative mechanism of Schweizer *et al.*[2] is generally operative, then the Wittig reaction between benzyltri-(2-furyl)phosphonium bromide (IX; R = $PhCH_2$) and benzaldehyde in anhydrous methanol containing sodium methoxide should lead to the vinylphosphonium salt (IV; Ar = 2-furyl, $R^1 = R^2 = Ph$, $R^3 = H$). On the basis of the established order of cleavage of groups from phosphorus in the alkaline hydrolysis of phosphonium salts, it was expected that the salt (IV; Ar = 2-furyl, $R^1 = R^2 = Ph$, $R^3 = H$) would undergo hydrolysis with *loss of furan* to give the oxide (X; $R^1 = R^2 = Ph$, $R^3 = H$). On the other hand, if the mechanism predominantly involved intramolecular collapse of the oxaphosphetan (II), the reaction would give tri-(2-furyl)phosphine oxide (V; Ar = 2-furyl) and stilbene.

Treatment of benzyltri-(2-furyl)phosphonium bromide with benzaldehyde in anhydrous methanol containing sodium methoxide led to the rapid formation of *trans*-stilbene (90%). The phosphine oxide (V; Ar = 2-furyl) was subsequently isolated in 95% yield. No other phosphine oxides were detected.

Similarly tri-(2-furyl)phosphine oxide (V; Ar = 2-furyl) was also isolated from the corresponding reaction of the ethylphosphonium salt (IX; R = Et, X = I); no other characterisable phosphorus-containing products could be isolated.

The above results indicate that the reactions follow the normal Wittig course involving collapse of an oxaphosphetan intermediate (II). A vinylphosphonium intermediate would not appear to be involved.

We have also studied the reactions of a series of methylphosphonium salts bearing 2-furyl substituents (IX; R = Me, X = I^-), (XI), and (XII), with benzaldehyde in ethanolic sodium ethoxide solution. Assuming the participation of a vinylphosphonium salt (IV; $R^1 = H$) in the reaction, it would be expected that preferential migration of the 2-furyl group from phosphorus to carbon might occur. (In the pinacol–pinacolone rearrangement, where the electronic situation is similar in that the migrating group is effectively carbanionic, it has been shown that a 2-furyl group migrates in preference to a phenyl group.[10])

In marked contrast to the reaction of methyltriphenylphosphonium iodide with benzaldehyde in ethanolic sodium ethoxide, which as indicated above gives predominantly the rearrangement product (VII; Ar = Ph, $R^1 = R^2 = H$, $R^3 = Ph$), the corresponding reaction of tri-(2-furyl)methylphosphonium iodide (IX; R = Me) gave the normal Wittig products, styrene and tri-(2-furyl)phosphine oxide (V; Ar = 2-furyl) in 50% yield. The expected rearrangement product (VII; Ar = 2-furyl, $R^1 = R^2 = H$, $R^3 = Ph$) was not detected.

Similarly, in the reactions of di-(2-furyl)methylphenylphosphonium iodide (XI) and (2-furyl)methyldiphenylphosphonium iodide (XII) with benzaldehyde under the same conditions as above, the normal Wittig products, di-(2-furyl)phenylphosphine oxide (XIII) (72%) and

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[7] S. Trippett and B. J. Walker, *J. Chem. Soc.*, 1966, 887.

[8] E. M. Richards and J. C. Tebby, *J. Chem. Soc.* (*C*), 1971, 1059.

[9] D. W. Allen, M. T. J. Mellor, and B. G. Hutley, *J.C.S. Perkin II*, 1972, 63.

[10] M. R. Kegelman and E. V. Brown, *J. Amer. Chem. Soc.*, 1953, **75**, 5961.

2-furyldiphenylphosphine oxide (XIV) (61%) together with styrene, were isolated. Once again, no rearrangement products were detected.

As for the benzyl- and ethyl-tri-(2-furyl)phosphonium salts discussed above, it would seem that the involvement of a vinylphosphonium salt is also unlikely in the Wittig reactions of methylphosphonium salts bearing 2-furyl substituents. These observations, together with those of Schweizer *et al.*[2] and Rakshys *et al.*,[5] support Trippett's recent suggestion that routes *via* oxaphosphetans (II) and vinylphosphonium salts (IV) are competitive; however the course taken depends not only on the nature of R^1, R^2, and R^3, but also on the nature of the substituents at phosphorus.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded using a JEOL 60 MHz spectrometer. G.l.c. analyses were carried out using a Pye series 104 chromatograph, equipped with a 5 ft column of Apiezon L on Celite, and a flame ionisation detector. T.l.c. separations were carried out on a preparative scale using a 0·5 mm thickness of Kieselgel HF 256 as adsorbent and ethyl acetate as solvent.

Preparation of Phosphonium Salts and Phosphine Oxides.—Tri-(2-furyl)phosphine was prepared and converted into benzyltri-(2-furyl)phosphonium bromide (IX; R = PhCH$_2$; X = Br) and methyltri-(2-furyl)phosphonium iodide (IX; R = Me; X = I) as described previously.[9] Treatment of the phosphine with ethyl iodide under reflux gave, after removal of the excess of ethyl iodide, and crystallisation of the residue from methyl acetate–ethanol, *ethyl-tri-*(2-*furyl*)*phosphonium iodide* (IX; R = Et, X = I), m.p. 122—123° (Found: C, 43·45; H, 3·6. $C_{14}H_{14}IO_3P$ requires C, 43·3; H, 3·6%), τ (CDCl$_3$) 1·84 (3H, m), 2·1 (3H, m), 3·1 (3H, m), 6·4 (2H, m), and 8·52 (3H, m). Oxidation of the phosphine with hydrogen peroxide in acetone gave tri-(2-furyl)phosphine oxide (V; Ar = 2-furyl), m.p. 115—117° (lit.,[11] 113—114°).

2-*Furyldiphenylphosphine.*—n-Butyl-lithium (0·3 mol) in light petroleum (b.p. 40—60°) (200 ml) was added dropwise, with stirring, under nitrogen, to furan (25 g, 0·3 mol) in ether (150 ml) during 20 min. The resulting solution was left for 1 h before being cooled in ice. Diphenylphosphinous chloride (22 g, 0·1 mol) in benzene (50 ml) was then added slowly. The mixture was then heated under reflux for 1 h, cooled in ice, and hydrolysed with ammonium chloride solution (10% w/v; 100 ml). The organic layer was then separated, dried (Na$_2$SO$_4$), and evaporated; the residue was distilled to give 2-*furyldiphenylphosphine* (16·2 g, 64%), b.p. 135° at 0·25 mmHg (Found: C, 76·3; H, 5·3. $C_{16}H_{13}OP$ requires C, 76·2; H, 5·15%). The phosphine, on treatment with methyl iodide gave 2-*furyl*(*methyl*)*diphenylphosphonium iodide* (XII), m.p. 159—160° (from MeOAc–EtOH) (Found: C, 51·95; H, 4·25. $C_{17}H_{16}IOP$ requires C, 51·75; H, 4·05%), τ (CF$_3$CO$_2$H) 1·92 (1H, m), 2·3 (10H, m), 2·7 (1H, m), 3·2 (1H, m), and 7·23 (3H, d, $^2J_{\mathrm{PCH}}$ 13·5 Hz). Oxidation of the phosphine with hydrogen peroxide in acetone gave 2-*furyldiphenylphosphine oxide* (XIV), m.p. 107—108° (from benzene–hexane) (Found: C, 70·9; H, 5·05. $C_{16}H_{13}O_2P$ requires C, 71·6; H, 4·85%). *Di*-(2-*furyl*)*phenylphosphine* was similarly prepared in 58% yield from n-butyl lithium (0·4 mol), furan (32 g, >0·4 mol), and phenylphosphonous dichloride (17·9 g, 0·1 mol), and had b.p. 112° at 0·15 mmHg (Found: C, 69·9; H, 5·25. $C_{14}H_{11}O_2P$ requires C, 69·45; H, 4·55%). Treatment of the phosphine with methyl iodide gave *di*-(2-*furyl*)*methylphenylphosphonium iodide* (XI), m.p. 151—152° (MeOAc–EtOH) (Found: C, 47·05; H, 3·65. $C_{15}H_{14}IO_2P$ requires C, 46·9; H, 3·65%), τ (CF$_3$CO$_2$H) 1·89 (2H, m), 2·2 (5H, m), 2·55 (2H, m), 3·12 (2H, m), and 7·2 (3H, d, $^2J_{\mathrm{PCH}}$ 14·85 Hz). On treatment with hydrogen peroxide in acetone, the phosphine gave *di*-(2-*furyl*)*phenylphosphine oxide* (XIII), m.p. 124—125° (from hexane–benzene) (Found: C, 65·25; H, 4·0. $C_{14}H_{11}O_3P$ requires C, 65·1; H, 4·25%).

Wittig Reactions of Methylphosphonium Salts.—These were carried out in duplicate, in dry ethanol, according to the following general procedure. The salt (10^{-3} mol) and freshly distilled benzaldehyde (10^{-3} mol), in dry ethanol (4 ml), were treated with ethanolic sodium ethoxide (10^{-3} mol) under nitrogen, and the resulting solution was left at room temperature for 7—14 days. The yield of styrene was then determined by g.l.c. and the involatile phosphine oxides present were separated by preparative t.l.c. and subsequently identified by comparison with the authentic substances. The compounds identified in the individual reactions, together with their yields, are listed below.

Tri-(2-*furyl*)*methylphosphonium iodide–benzaldehyde.* This reaction gave styrene (42%) and tri-(2-furyl)phosphine oxide (50%); in addition, di-(2-furyl)methylphosphine oxide (18%) was isolated, having presumably arisen from the very rapid hydrolysis of the original salt in the presence of a trace of water in the ethanolic ethoxide medium.

Di-(2-*furyl*)*methylphenylphosphonium iodide–benzaldehyde.* This reaction gave styrene (74%) and di-(2-furyl)phenylphosphine oxide (72%).

2-*Furyl*(*methyl*)*diphenylphosphonium iodide–benzaldehyde.* This reaction gave styrene (53%) and 2-furyldiphenylphosphine oxide (61%).

Wittig reaction of benzyltri-(2-*furyl*)*phosphonium bromide with benzaldehyde.* The salt (10^{-3} mol) and benzaldehyde (10^{-3} mol) in dry methanol (3—4 ml), were treated with sodium methoxide (10^{-3} mol) in methanol, under nitrogen. After a few seconds, *trans*-stilbene crystallised. From the mother liquor, a further quantity of *trans*-stilbene was isolated giving a total yield of 95%, together with tri-(2-furyl)phosphine oxide (0·224 g, 95%). T.l.c. indicated the absence of other phosphine oxides.

Wittig reaction of ethyltri-(2-*furyl*)*phosphonium iodide with benzaldehyde.* The reaction was carried out as described above, on a 10^{-3} molar scale. The sole phosphine oxide product isolated was tri-(2-furyl)phosphine oxide (40%).

[2/2529 *Received, 8th November,* 1972]

[11] C. E. Griffin, R. P. Peller, K. R. Martin, and J. A. Peters, *J. Org. Chem.*, 1965, **30**, 97.