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# THE EFFECTS OF STERIC CROWDING AT PHOSPHORUS IN WITTIG REACTIONS OF SEMISTABILISED YLIDES IN ETHANOL. EVIDENCE FOR A CYCLOADDITION MECHANISM

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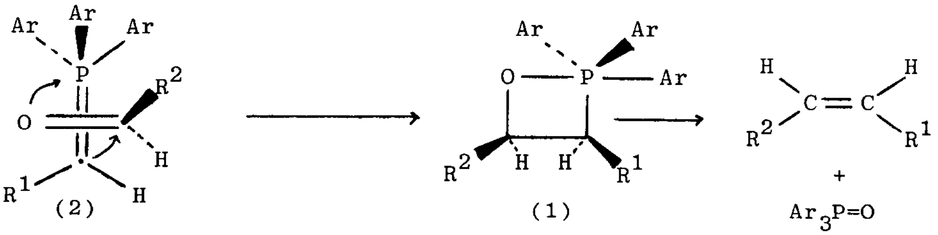
*Summary: Increasing steric crowding at phosphorus in Wittig reactions of semistabilised phosphonium ylides in ethanol leads to an increase in the cis-trans ratio of the resulting alkenes, suggesting the involvement of a cycloaddition mechanism and the non-involvement of betaine intermediates.*

In recent years, evidence has been presented that 1,2-oxaphosphetans are formed directly in the Wittig reactions of phosphonium ylides and carbonyl compounds, without the intermediacy of the commonly assumed phosphonium betaines. $^{31}P$ nmr studies on solutions in THF of non-stabilised ylides and carbonyl compounds under salt-free conditions clearly indicate the presence of intermediate oxaphosphetans only.[1,2] Studies of the kinetics of reactions of stabilised ylides with carbonyl compounds in non-polar aprotic solvents and also in glycols are also consistent with the concept of a highly oriented transition state of low polarity.[3-6]

The preferential formation of cis-alkenes in the Wittig reactions of non-stabilised ylides in THF has been attributed to the initial formation of the cis-1,2-oxaphosphetan (1) via a transition state (2) involving orthogonal approach of the P=C double bond of the ylide and the carbonyl bond in a $\pi_{2a} + \pi_{2s}$ cycloaddition reaction.[1]



A cycloaddition mechanism has also been proposed recently in order to account for the influence of electron-withdrawing and -donating substituents at phosphorus on the reactivity of stabilised triarylphosphonium ylides towards substituted benzaldehydes in acetonitrile solution.[7]

In extension of our studies on factors affecting the course of the Wittig reaction in protic solvents,[8] we have now investigated the influence of a range of substituted aryl groups at phosphorus on the stereochemistry of alkene formation in the reactions of the semistabilised ylides (3) with benzaldehyde in ethanol, using ethoxide as base. Our results imply the direct formation of 1,2-oxaphosphetan intermediates (1) under conditions which might have been expected to promote the formation of betaine intermediates.

$$\underset{(3)}{Ar^1_2Ar^2P{=}CHPh} + PhCHO \xrightarrow[EtO^-Na^+]{EtOH} Ar^1_2Ar^2P{=}O + PhCH{=}CHPh$$

Earlier studies of the influence of the substituents at phosphorus on the stereochemistry of the resulting alkene have been interpreted in terms of the involvement of betaine intermediates.[9-15] The presence of electron-withdrawing groups[11] (e.g. p-chlorophenyl) or a small ring system at phosphorus[14] are said to favour betaine collapse, such that a greater proportion of the *cis*-alkene arising from the *erythro*-betaine is formed. Conversely, electron-donating groups (e.g. p-methoxyphenyl) reduce the rate of betaine collapse, thereby favouring the predominant formation of the *threo*-betaine and in turn the *trans*-alkene. Related studies have shown that the *cis*-*trans* ratio is also dependent on the nature of the solvent, protic solvents favouring the *trans*-isomer, perhaps as a result of reducing the rate of betaine collapse by hydrogen bonding with the betaine oxygen.[15]

The results of our experiments[16] are summarised in the Table.

Table

Cis-trans Ratios and Total Yields of Stilbenes from the Reaction of the Ylides $Ar^1_2Ar^2P{=}CHPh$ with Benzaldehyde in Ethanol

| Ylide | cis-trans ratio (%) | total yield of stilbenes, % |
|---|---|---|
| (a) $Ar^1 = Ar^2 = Ph$ | 40 60 | 60 |
| (b) $Ar^1$ = Ph; $Ar^2$ = *o*-tolyl | 62:38 | 69 |
| (c) $Ar^1$ = *o*-tolyl; $Ar^2$ = Ph | 67·33 | >95 |
| (d) $Ar^1 = Ar^2$ = *o*-tolyl | 70·30 | 76 |
| (e) $Ar^1 = Ar^2$ = p-tolyl | 42:58 | >95 |
| (f) $Ar^1$ = Ph; $Ar^2$ = *o*-chlorophenyl | 70:30 | 69 |

It is apparent that increasing steric crowding about phosphorus results in an *increase* in the cis-trans ratio. The comparison between the tris-p-tolyl- and the tris-o-tolyl ylides is very marked, and even one o-tolyl group has a significant effect. Both steric and electronic effects of these groups would have been expected to favour formation of the trans-alkene in terms of the betaine mechanism, since the rate of betaine collapse would be reduced. A similar increase in cis-trans ratio is found for the o-chlorophenyl substituent.

In this case, both steric and electronic effects would seem to be operating in the same direction, and it is interesting to note that one o-chloro substituent has the same effect as three o-methyl groups.

We suggest that the increase in the cis-trans ratio on increasing steric crowding at phosphorus clearly points to the involvement of a cycloaddition mechanism of the type suggested by Vedejs and Snoble.[1] An increase in steric crowding at phosphorus will favour a transition state (2) in which group $R^2$ is directed away from the phosphorus substituents, leading directly to the 1,2-oxaphosphetan (1) and hence to the cis-alkene.

It has been suggested recently[7] that the predominant formation of trans-alkenes in Wittig reactions of stabilised ylides can also be accounted for in terms of a cycloaddition mechanism involving the coplanar combination of P=C and C=O, in a $\pi_{2s} + \pi_{2s}$ cycloaddition mode. Doubtless the formation of the trans-alkene in the reactions of the above semistabilised ylides can be similarly explained.

An alternative explanation[17] of the above results could be that increased steric crowding causes reduced solvation at phosphorus which might therefore be expected to *increase* the rate of betaine collapse, and thereby favour the cis isomer. Such a solvation effect is analogous to the change produced in passing from protic to aprotic solvent in that the o-methyl groups reduce the local polarity of the solvent near the reaction centre. However, in the alkaline hydrolysis of phosphonium salts, it has been shown that while a change from protic to aprotic solvent markedly increases the rate of the hydrolysis reaction[18] due to decreased solvation, the effects of increasing steric crowding lead to a *decrease* in the rate of nucleophilic attack at phosphorus, both in phosphonium salt hydrolysis[19] and also in phosphonium betaine collapse.[8]

We are now exploring both the steric and electronic effects of the substituents at phosphorus on the stereochemistry of alkene formation in Wittig reactions involving fully stabilised, and reactive ylides.

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16. The reactions were carried out by dissolving the appropriate benzylphosphonium salt (1.25 x $10^{-4}$ moles) and benzaldehyde (1.25 x $10^{-4}$ moles) in dry ethanol (2.5 cm$^3$) containing sodium ethoxide (1.25 x $10^{-4}$ moles). After 1 hr at room temperature, the solutions were diluted with toluene (2.5 cm$^3$) and analysed for *cis*- and *trans*-stilbene by GLC. (5' SE30 on celite at 205°, using a flame ionisation detector). No attempt was made to optimise overall yields of alkenes.
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