Tetrahedron Letters No. 19, pp 1787 - 1790, 1974. Pergamon Press. Printed in Great Britain.

STERIC AND ELECTRONIC EFFECTS OF SUBSTITUENTS AT PHOSPHORUS ON THE COURSE OF THE WITTIG REACTION IN PROTIC SOLVENTS

David W. Allen*, Phillip Heatley, Barrie G. Hutley and Malcolm T.J. Mellor
Department of Chemistry and Biology, Sheffield Polytechnic, Pond Street,
Sheffield S1 1WB.

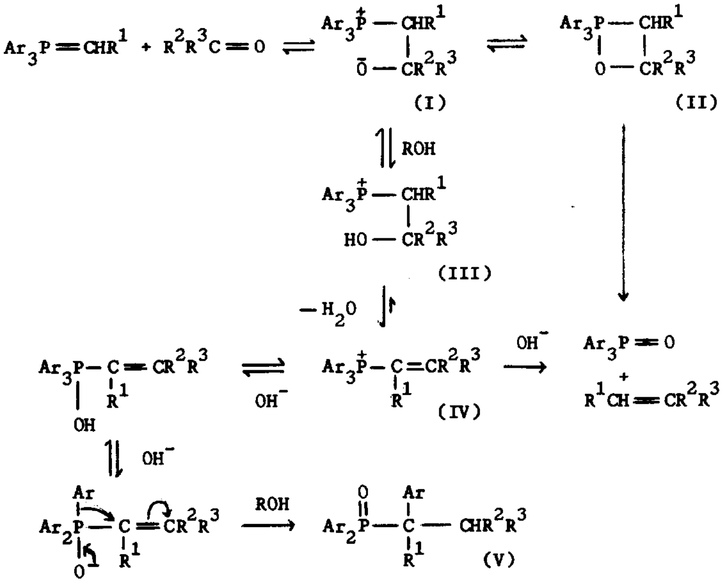
(Received in UK 28 March 1974; accepted for publication 4 April 1974)

The Wittig reaction between a phosphonium salt and a carbonyl compound in the presence of alkoxide ion in protic solvents may occur by two competing mechanistic courses (see Scheme). On the one hand, the initially formed betaine (I) may undergo rate-determining collapse to the normal Wittig products (i.e. olefin and phosphine oxide) via a four-membered cyclic oxaphosphetan (II)[1]. Alternatively, protonation of the betaine may occur to give the β-hydroxyalkylphosphonium salt (III) which subsequently may eliminate water to form the vinylphosphonium salt (IV). Hydrolysis of the latter may then occur <u>either</u> with cleavage of the vinylic substituent to give the normal Wittig products[2] <u>or</u> with migration of an aryl group from phosphorus to adjacent carbon to form the rearrangement product (V)[3]. The preferred course has been shown to depend on

(i) the nature of the substituents R^1, R^2, and R^3 [2-4]

and (ii) the electron-withdrawing character of the substituents at phosphorus[5].

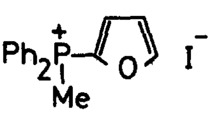
The presence of bulky groups at phosphorus has been shown to have a marked influence on the course of alkaline hydrolysis of phosphonium salts; in such crowded systems, loss of the substituent which forms the most stable carbanion may not necessarily occur[6]. Since both competing routes for the Wittig reaction in protic solvents involve nucleophilic attack at a phosphonium centre, we have studied the effect of introducing bulky groups at phosphorus



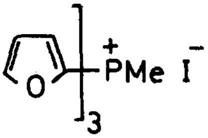
Scheme

both on the preferred mechanistic course and the resulting products of such reactions.

The reaction of methyltriphenylphosphonium iodide and benzaldehyde in ethanolic sodium ethoxide yields predominantly the rearrangement product (V, Ar = R^3 = Ph; R^1 = R^2 = H) via a vinylphosphonium intermediate.[3,7] In contrast, the analogous reactions of the phosphonium salts (VI and VII) yield the normal Wittig products, styrene and the phosphine oxides (VIII) and (IX) respectively.[5] It was suggested on the basis of earlier work[8] that the 2-furyl substituents act as electron-withdrawing groups which favour intramolecular collapse of the betaine (I). Introduction of a t-butyl group at phosphorus has a further major effect on the course of such reactions. The major product of the reaction of the salt (X) with benzaldehyde in ethanolic ethoxide is the *vinylphosphine oxide* (XI) m.p. 104° (m/e 274, M^+) arising by loss of furan[9] from a vinylphosphonium intermediate.



(VI)



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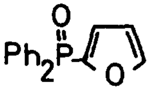

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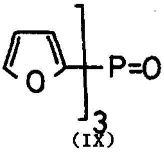

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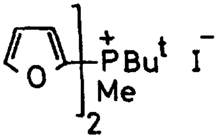
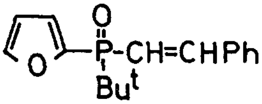


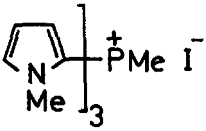
(X)



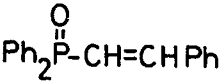
(XI)

Replacement of the 2-furyl substituents in the salts (VI) and (VII) by the 2-(1-methylpyrrolyl) group has a similar effect. Thus the salts (XII) and (XIII) give the vinylphosphine oxides (XIV) (m.p. 168°, lit[10] 168-9°) and (XV) (m/e 310, M^+) respectively, with loss of 1-methylpyrrole.[9]

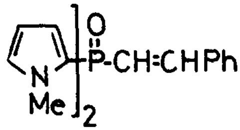
(XII)



(XIII)



(XIV)



(XV)

Clearly a very delicate balance of steric and electronic effects controls the course of Wittig reactions conducted in protic solvents. In our studies of the alkaline hydrolysis of heteroarylphosphonium salts, we have shown that while the forming 2-(1-methylpyrrolyl) carbanion is less stable than 2-furyl, it is nevertheless more stable than the forming phenyl carbanion.[11] Thus hydrolysis of the salt (XII) occurs with exclusive loss of 1-methylpyrrole.[9] In addition, it would seem reasonable to suppose that the 2-(1-methylpyrrolyl) group is somewhat more bulky than the 2-furyl. The ultimate fate of the phosphobetaine (I) is determined by the relative rates of the intramolecular collapse and dehydration steps. The bulky t-butyl group inhibits intramolecular collapse and allows the dehydration step to occur. The 2-(1-methylpyrrolyl) group similarly reduces the rate at which intramolecular collapse occurs, and the dehydration step is again favoured. The decomposition of the vinylphosphonium intermediate (IV) leading to abnormal products depends on the carbanionic stability of the group cleaved from phosphorus. Carbanions of moderate stability such as phenyl require the additional stabilisation of negative charge afforded in the transition state of the rearrangement reaction. For carbanions of greater stability, such as the 2-heteroaryl carbanions, simple cleavage of the leaving group can occur.

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