The Fate of Phosphobetaines in Protic Solvents

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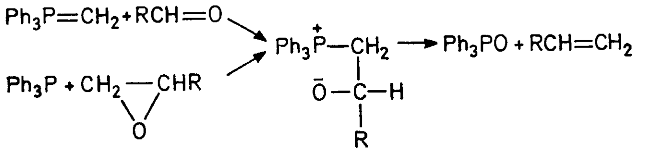
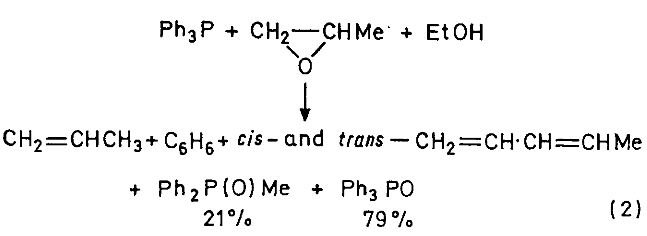
Summary Reactions in protic solvents of 2-hydroxyalkyltriphenylphosphonium salts with base and of triphenylphosphine with propylene oxide produce numerous unexpected products, thereby revealing a much wider scope of reactivity for the phosphobetaine intermediates of these reactions than was previously recognized.

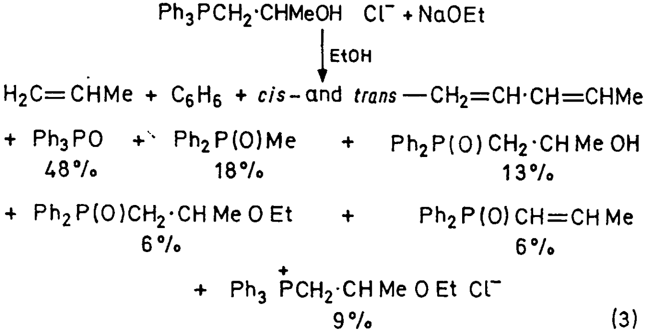
PHOSPHOBETAINES (I) the intermediates in both Wittig reactions and phosphine–epoxide reactions, undergo a well documented[1] decomposition in aprotic solvents to an olefin and a phosphine oxide (Equation 1). However, the fate of the betaine (I) in protic solvents has received less attention,[2,3] and we report findings which demonstrate a much wider scope of reactivity for compound (I) in such media than was recognized previously, as shown by the numerous products observed for reactions (2)—(4) in addition to the expected products, triphenylphosphine oxide and propylene (or ethylene).



(I) (1)

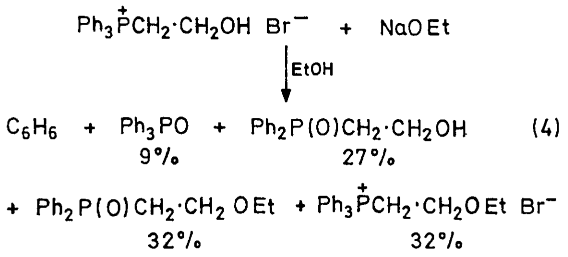
In reaction (2), triphenylphosphine and a twofold excess of propylene oxide were heated at 100 °C for 1 h in ethanol. The mixture was then separated into volatile and non-volatile fractions. The non-volatile fraction was quantitatively separated by p.l.c. into the two phosphine oxides in the amounts indicated.† The volatile fraction was found to consist of the other products shown in addition to unchanged propylene oxide and ethanol. Diphenylmethylphosphine oxide, benzene, and the penta-1,3-dienes were shown to be formed in the molar ratio 1 : 1 : 0·5, and equal amounts of *cis*- and *trans*-1,3-pentadiene are produced.





$$\mathrm{Ph_3\overset{+}{P}CH_2{\cdot}CHMeOH\ Cl^- + NaOEt} \xrightarrow{\mathrm{EtOH}} \mathrm{H_2C{=}CHMe + C_6H_6} + cis\text{- and } trans\mathrm{{—}CH_2{=}CH{\cdot}CH{=}CHMe}$$
$$+ \underset{48\%}{\mathrm{Ph_3PO}} + \underset{18\%}{\mathrm{Ph_2P(O)Me}} + \underset{13\%}{\mathrm{Ph_2P(O)CH_2{\cdot}CHMeOH}} + \underset{6\%}{\mathrm{Ph_2P(O)CH_2{\cdot}CHMeOEt}} + \underset{6\%}{\mathrm{Ph_2P(O)CH{=}CHMe}} + \underset{9\%}{\mathrm{Ph_3\overset{+}{P}CH_2{\cdot}CHMeOEt\ Cl^-}} \qquad (3)$$

In reactions (3) and (4), the phosphonium salt and a twofold excess of sodium ethoxide were stirred for 2 h at 25 °C in ethanol. These reactions were analysed as above.



$$\mathrm{Ph_3\overset{+}{P}CH_2{\cdot}CH_2OH\ Br^- + NaOEt} \xrightarrow{\mathrm{EtOH}} \mathrm{C_6H_6} + \underset{9\%}{\mathrm{Ph_3PO}} + \underset{27\%}{\mathrm{Ph_2P(O)CH_2{\cdot}CH_2OH}} \qquad (4)$$
$$+ \underset{32\%}{\mathrm{Ph_2P(O)CH_2{\cdot}CH_2OEt}} + \underset{32\%}{\mathrm{Ph_3\overset{+}{P}CH_2{\cdot}CH_2OEt\ Br^-}}$$

Reactions (2)—(4) presumably involve phosphobetaine intermediates (I) and probable mechanisms for their further transformation into their respective products are outlined in the Scheme. Although several of the individual reactions in this Scheme have been considered by previous workers,[1,2,4–6] clarification of the reaction pathways leading to such a diversity of product was still needed. An understanding of the reactions of a betaine (I) in a protic solvent requires consideration

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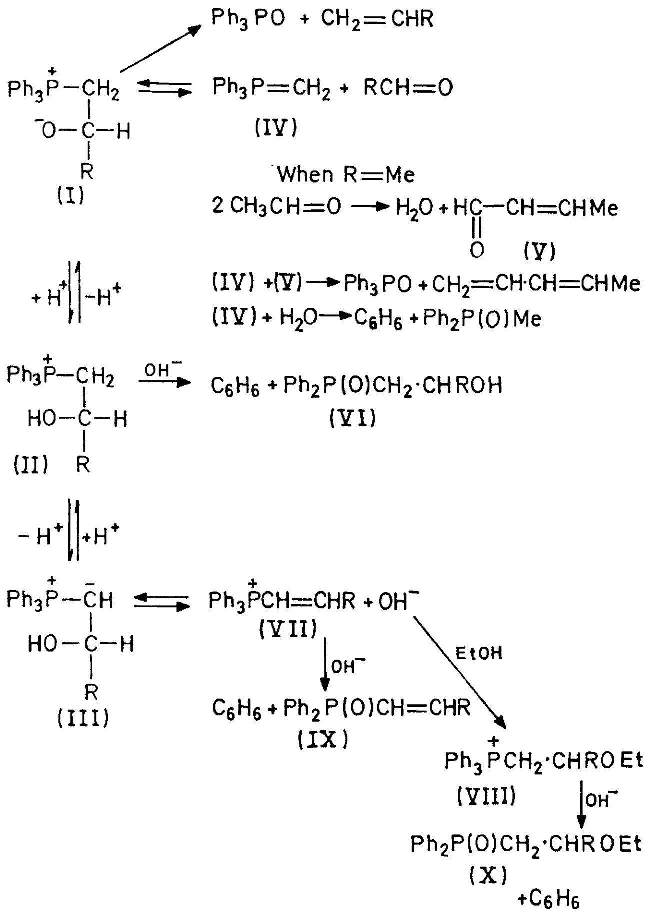
† The compounds were identified by their n.m.r. and mass spectra, m.p., and elemental analyses. Small amounts (<5%) of other compounds could have also been present but escaped detection.

of the reactivity of its tautomer (III) and of its conjugate acid (II). Compound (I) can react either in the usual Wittig manner to form an olefin and triphenylphosphine oxide, or it can decompose reversibly to triphenylmethylenephosphorane (IV) and an aldehyde.[4,5] It is likely, however, that in the basic protic medium, further reactions of both compound (IV) and the aldehyde compete with their recombination.[7] For example, *cis-* and *trans*-penta-1,3-diene and diphenylmethylphosphine oxide are probably formed by a series of reactions in which acetaldehyde undergoes base-catalysed condensation and dehydration to form the unsaturated aldehyde (V) and water,[8] and these products react further with the phosphorane (IV) as indicated in the Scheme.



SCHEME

The reactions of the ylide (III) are undoubtedly initiated by loss of hydroxide, giving the vinylphosphonium salt (VII).[2] The versatile intermediate (VII)[2,6] can add ethoxide to form, after protonation, a new phosphonium salt (VIII) or can react with hydroxide to form benzene and a diphenylvinylphosphine oxide (IX). The salt (VIII) can also react further with hydroxide to form benzene and the corresponding phosphine oxide (X). The isolation of (X; R=H) as the only phosphorus-containing product from the decomposition of 2-hydroxyethyltriphenylphosphonium bromide by ethanolic sodium ethoxide has been reported by Hands and Mercer,[3] who suggested a reaction mechanism involving direct attack of ethoxide on the betaine (I) in the product-forming step. Our scheme differs fundamentally from their mechanism in that we invoke a vinylphosphonium salt intermediate. The isolation of (VIII) and (IX) lends strong support to this suggestion. Finally, to complete the Scheme, the reaction of the intermediate (II) with hydroxide generated in the reactions of the betaines (I) or (III) yields benzene and the oxide (VI).

An interesting feature of reactions (2) and (3) is that equal amounts of *cis-* and *trans*-penta-1,3-diene are formed, in spite of the fact that the aldehyde precursor (V) is known only in the *trans*-form[8] (*i.e.*, crotonaldehyde). This observation is important since it requires that at least equal amounts‡ of *cis-* and *trans*-(V) are formed in the dehydration of the aldol, and its generality deserves further study since it is usually thought[9,10] that formation of the *trans*-isomer is favoured in such a reaction.

The product distribution is quite different for the three reactions (Equations 2—4). For example, whereas most of the products observed when R=Me (Equations 2 and 3) are derived from the betaine (I) the products from (II) and (III) predominate when R=H (Equation 4). The interpretation of these differences is the key to a detailed understanding of this very complex system.

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‡ We cannot exclude the possibility that even larger amounts of the *cis*-isomer are formed but partially isomerize to the thermodynamically favoured *trans*-isomer before reacting with (IV) thereby fortuitously yielding equal amounts of *cis-* and *trans*-penta-1,3-dienes.

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