Reversibility of a Wittig Intermediate derived from a Triphenylphosphonium Ylide and an Aliphatic Aldehyde

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Wittig-reaction intermediates derived from hexanal and (γ-oxidopropylidene)triphenylphosphorane, (**1**), are freely reversible, as indicated by significant quantities of cross-over products from a second aldehyde (octanal); such a result may account for anomalously enhanced *E* stereoselectivity in the reaction of γ- and β-oxido ylides with aliphatic aldehydes.

Wittig-reaction intermediates generated by combining non-stabilized triphenylphosphonium ylides and aldehydes have been shown to be primarily oxaphosphetanes [*e.g.*, (**2a**) and (**2b**)] by ^{31}P n.m.r. spectroscopy.[1,2] Those intermediates derived from aromatic aldehydes are formed reversibly, as demonstrated by trapping of the ylide arising from preformed adducts with a second aldehyde (cross-over),[1,3] and observation of 'stereochemical drift' over the reaction course by ^{31}P n.m.r. spectroscopy.[2] Thus, a measure of thermodynamic control is imparted to such Wittig reactions. However, reversal *does not* occur with adducts derived from aliphatic aldehydes.[1–4]† We now report the first instance of reversibility for a non-stabilized triphenylphosphonium ylide and an aliphatic aldehyde, involving the reaction of (γ-oxidopropylidene)triphenylphosphorane, (**1**), and hexanal. This finding is relevant to the mechanism by which ylides with anionic substituents yield an exaggerated amount of *E* alkene.[6]

A solution of ylide (**1**) [0.25 M in tetrahydrofuran (THF)], prepared from the corresponding bromide salt[7] and 2.2 mol equiv. of $LiN(SiMe_3)_2$, was mixed with 2 mol equiv. of hexanal at −55 °C (see Scheme 1). After stirring for 10 min, with care to ensure the dissolution of the hexanal, the red ylide colour was largely dissipated. Octanal (5 mol equiv.) was added and the solution was stirred for 5 min, then allowed to warm slowly to 23 °C. The reaction mixture was treated with water and extracted into diethyl ether. We analysed the alkene mixture by g.l.c.–mass spectroscopy and by g.l.c.‡ The g.l.c. peaks were compared with alkenes prepared independently (as purified isomeric mixtures) by the Wittig reaction.§ In the cross-over experiment, a 45:55 *Z*/*E* mixture of hexanal-derived products, (**3a**)/(**3b**), in 25% yield, and a 33:67 *Z*/*E* mixture of octanal-derived alkenes, (**5a**)/(**5b**), in 35% yield, were observed. The ratio of cross-over to normal products of 1.4:1 indicates a large degree of reversibility associated with

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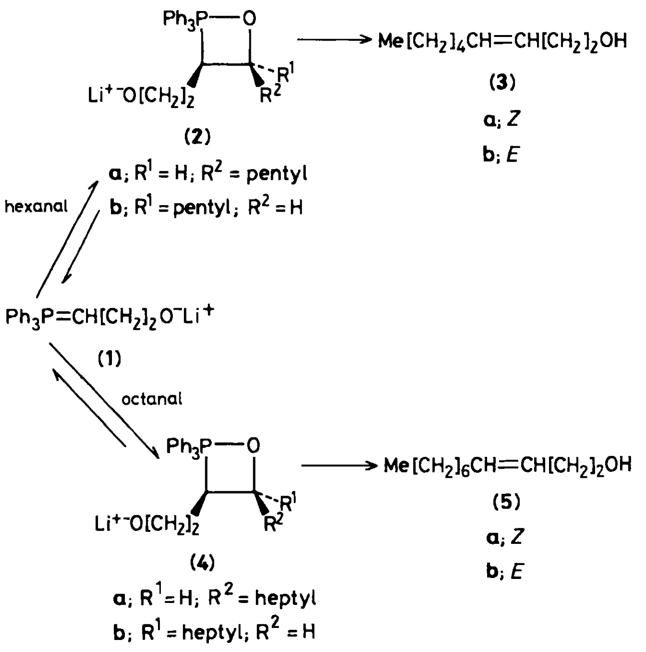
† Vedejs recently reported cross-over for a diphenylalkyl *moderated* ylide [diphenylmethyl-(2-methylprop-2-enylidene)phosphorane] with aliphatic aldehydes (ref. 5).

‡ Chemical ionisation mass spectroscopy (CH_4) of the alkenes showed that the pairs (**3a**)/(**3b**) and (**5a**)/(**5b**) were isomeric with the expected molecular weights. G.l.c. quantitation (on a 10% Carbowax on Chromosorb column) was conducted by using detector response factors relative to diphenylmethane as an internal reference, assuming that ratios of detector response factors for isomeric pairs, (**3a**)/(**3b**) and (**5a**)/(**5b**), were unity.

§ Alkene ratios in the independent synthesis were: (**3a**)/(**3b**) = 41:59 and (**5a**)/(**5b**) = 39:61. Alkene mixtures (**3**) and (**5**) were separately characterized by ^{1}H and ^{13}C n.m.r. spectroscopy.



Scheme 1

oxaphosphetanes (**2**) and (**4**). (Similar results were found in three separate experiments.)

Although it is conceivable that a positive cross-over result might arise from failure of the first reaction to take place, Wittig intermediates of the type discussed here are formed instantaneously at low temperatures (−50 to −80 °C);[1,2] also, the excess of the first aldehyde used would encourage complete adduct formation. In any event, we conducted some ^{31}P n.m.r. studies (in THF) to illuminate this issue. The broad-band proton-decoupled ^{31}P n.m.r. spectrum (145.8 MHz) of (**1**) revealed a wide envelope of peaks between 5 and 25 p.p.m. (relative to external 85% H_3PO_4), similar to the spectrum described for a related β-oxido ylide.[8] In the reaction of (**1**) with benzaldehyde or hexanal (2 mol equiv.) at *ca.* −50 °C, oxaphosphetanes were formed as judged by resonances attributable to such species between −60 and −65 p.p.m.[1,2] In these experiments a small amount of ylide (generally 5—15% of total phosphorus species) was observed, but it is impossible to ascertain directly whether the ylide derives from incomplete reaction or from a role in a rapid equilibration process. Based on the measured amount of cross-over products, at least 0.35 mol equiv. of unreacted ylide (**1**) is required subsequent to addition of the first aldehyde. This circumstance is very unlikely because of the ^{31}P n.m.r. results, and the reactivity properties observed for related ylide (**6**) (*vide infra*), as for well as typical non-stabilized ylides.[1,2]

$$Ph_3P{=}CH[CH_2]_3CO_2{}^-M^+$$

(**6**)

Ylides in which an oxido group is proximal to the phosphorus atom demonstrate, in reactions with both aliphatic and aromatic aldehydes, anomalous *E* stereoselectivity, which is not largely associated with equilibration of Wittig intermediates by intramolecular proton-exchange processes.[6,9,10] The carboxy ylide (**6**) is interesting in that it exhibits stereoselectivity in reactions with aromatic, *but not aliphatic,* aldehydes.[10] A cross-over experiment with (**6**) and nonanal, followed by octanal, under the conditions described above, generated virtually no (<1%) cross-over products. Thus, we propose that it is the *reversibility* of Wittig intermediates derived from (**1**) and aliphatic aldehydes that distinguishes such adducts from those in more typical Wittig reactions, and allows (**1**) to display anomalous *E* stereoselectivity. This principle, which readily extends to Wittig reactions of (**1**) and aromatic aldehydes, reasonably accounts for the anomalous *E* stereoselectivity of γ- and β-oxido ylides. Ylides bearing more mildly nucleophilic groups, such as (**6**), may yet enhance the reversibility process with aromatic aldehydes, but they are unable to do so with aliphatic aldehydes, whereupon the usual preponderance of *Z* alkene is found.[10]

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