Stereochemically Pure *E*- and *Z*-Alkenes by the Wittig–Horner Reaction

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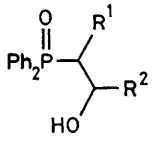
Summary Pure *Z*-alkenes are obtained stereospecifically from *erythro*-alcohols (**3**) formed on addition of Ph_2PO-stabilised anions to aldehydes; acylation of the same anions, reduction of the α-$Ph_2P(O)$ ketones (**5**) to the *threo*-alcohol (**6**), and elimination gives pure *E*-alkenes.

THE regiospecificity of the Wittig reaction makes it first choice for many alkene syntheses. Although progress has been made in improving stereochemical control,[1] this remains a problem since mixtures of *E*- and *Z*-isomers are usually produced. In non-polar solvents, stabilised ylides give mainly *E*-alkenes whilst non-stabilised ylides give mainly *Z*-alkenes, but some of the other isomer is also formed and separation is often difficult.

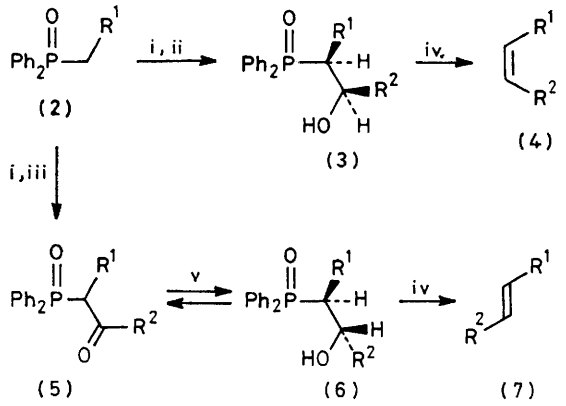
We believe that the Wittig–Horner modification using diphenylphosphinoyl (Ph_2PO) as the anion-stabilising

group has definite advantages over the conventional Wittig reaction.[2] The reaction stops with the formation of the alcohols (**1**); these are stable, crystalline compounds easily separated into pure diastereoisomers by chromatography (t.l.c., flash column,[3] or h.p.l.c.) and crystallisation. The two diastereoisomers of (**1**) are formed with high stereoselectivity by simple reactions (Scheme), and elimination of the water-soluble Ph_2PO^- from the anion (NaH) of (**1**) to give the alkene is stereospecific.†

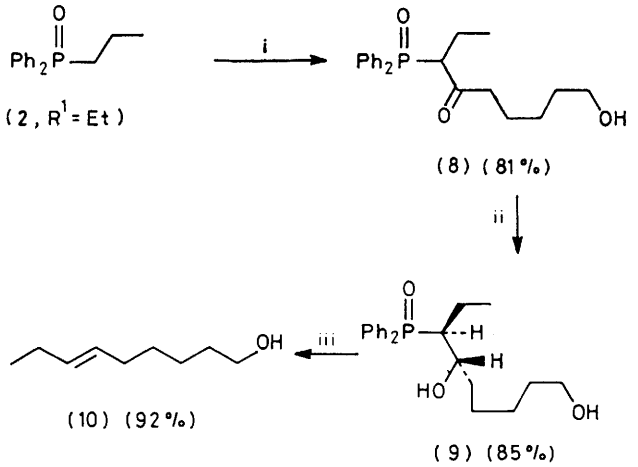


(1)

Z-Alkenes may be prepared as follows. Lithium derivatives of alkyl diphenylphosphine oxides (**2**) [Bu^nLi, tetrahydrofuran (THF), −78 °C] add to aldehydes giving predominantly *erythro*-alcohols (**3**, *e.g.* R^1 = Me, R^2 = 3,4-methylenedioxyphenyl, 9 : 1, 75% pure *erythro* isolated) in good yields (54—77%). Flash column chromatography and crystallisation gives pure *erythro*-(**3**). Elimination [NaH, dimethylformamide (DMF), 50 °C] gives the *Z*-alkene (**4**, *e.g.* α-isosafrole, R^1 = Me, R^2 = 3,4-methylenedioxyphenyl, 84%).‡



SCHEME. Reagents: i, Bu^nLi, THF, −78 °C; ii, R^2CHO; iii, R^2CO_2Et or $CH_2[CH_2]_nOC=O$; iv, NaH, DMF; v, $NaBH_4$; vi, [O].



Reagents: i, Bu^nLi, THF, −78 °C, then $CH_2[CH_2]_4OC=O$; ii, $NaBH_4$, EtOH; iii, NaH, DMF.

E-Alkenes may be prepared as follows. Alkyl diphenylphosphine oxides (**2**) are acylated (Bu^nLi, THF, −78 °C) with carboxylate esters or lactones giving α-Ph_2PO ketones (**5**) (64—85%). Reduction ($NaBH_4$, EtOH) of the ketones, *e.g.* (**8**), gives predominantly *threo*-alcohols (**6**),[4] *e.g.* (**9**; 6 : 1) in excellent yields (75—91%). Purification of the alcohols and elimination as before gives pure *E*-alkenes (**7**). A component (**10**) of the male Mediterranean fruit fly pheromone[5] was made by this method; the *Z*-isomer could not be detected by n.m.r. or g.l.c.

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† An *X*-ray crystal structure of the major alcohol obtained by addition of the lithium derivative of (**2**) (R^1 = Me) to benzaldehyde confirmed the assignment of the *erythro*-configuration (**3**, R^1 = Me, R^2 = Ph) (W. B. Cruse and O. Kennard, unpublished observations).

‡ When R^1 or R^2 = aryl, trace amounts of the *E*-alkene were detected by g.l.c.

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[5] M. Jacobson, K. Ohinata, D. L. Chambers, W. A. Jones, and M. S. Fujimoto, *J. Med. Chem.*, 1973, **16**, 248.