Dichotomous Ylide Formation from an Alkyl(benzyl)phosphonium Salt Leading to Stereoselective Alkene Syntheses

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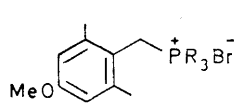
Condensation reactions between the tributyl-(4-methoxy-2,6-dimethylbenzyl)phosphonium salt (1b) and several aryl alkyl ketones, in the presence of methylsulphinylmethanide ion, are shown to lead to mixtures of stilbene and styrene products, resulting from dichotomous ylide formation. By contrast, with *p*-anisaldehyde, the salt (1b) produces solely the stilbene (10), and condensation between the tributyl-(4-methoxybenzyl)phosphonium salt (8) and 4′-methoxyacetophenone produces only the stilbene (9). The olefin-forming reactions between (1b) and aryl alkyl ketones are completely stereoselective, leading to *Z*-stilbenes [*e.g.* (3)] and *E*-styrenes [*e.g.* (6)]. Explanations for the stereoselectivities are discussed.

The Wittig reaction is probably the most versatile olefin synthesis known. Its advantages and convenience over other carbon–carbon bond forming reactions have been stressed.[1] In the preceding paper we described the application of benzylic phosphonium ylide intermediates in the syntheses of sterically crowded stilbenes. During these studies we observed unprecedented limitations to the 'normal' Wittig synthesis which led us to examine certain features of the reaction in greater detail.

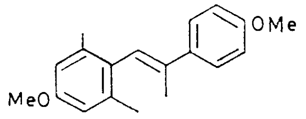
We have shown that condensation between the ylide from the salt (1a) and 4′-methoxyacetophenone gives only *ca.* 2% of stilbenes [(2) + (3)] with trimethylanisole (4) as the major product (*ca.* 50%). Use of elevated temperatures and an excess of carbonyl compound increases the yield of stilbene to *ca.* 25%. An alternative way of increasing the yield of stilbenes [(2) + (3)] appeared to be the application of the corresponding tributylphosphonium salt (1b). The ylide from this salt is expected to be more nucleophilic, and the smaller n-butyl groups provide less steric hindrance in the transition states. Indeed, condensation between the salt (1b) and 4′-methoxyacetophenone did give a greater yield of stilbene product, but the course of the reaction was particularly interesting.

Chromatography separated three products, identified as the stilbene (3) (29%), the hydrolysis product (4) (37%), and the styrene (6) (14%). Surprisingly the olefin-forming reactions leading to (3) and (6) were both totally stereoselective, giving the *Z*-stilbene and the *E*-styrene. Chromatography and spectral data did not detect the presence of the corresponding isomeric olefins. The configuration assigned to the stilbene product followed from comparison of spectral data with those of the authentic *E*-isomer (2) and also from the observation that it produced the *E*-isomer (2) upon isomerisation in the presence of iodine. The configuration assigned to the styrene (6) also followed from comparison of spectral data with those of the *Z*-isomer (7). Paradoxically, a Wittig condensation between triphenylphosphonium butylide and 4′-methoxyacetophenone, under similar conditions, produced largely the *Z*-styrene (7) (*Z* : *E* ratio 9 : 1).

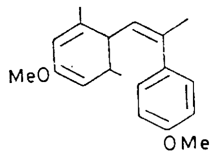
The styrene (6) is produced as a result of intermediate formation of the ylide (5) from the benzyl salt (1b). To our knowledge this is the first time that dichotomous ylide formation has been observed from an alkyl(benzyl)phosphonium salt. This observation clearly reflects the diminished acidity of the benzylic C–H bonds in (1b) over those in other benzyl salts, presumably as a consequence of the steric influence of the proximate *ortho*-methyl groups in (1b). A similar condensation between the salt (8), lacking *ortho*-methyl substitution, and 4′-methoxyacetophenone produced the stilbene (9) uncontaminated with the styrene (6). With *p*-anisaldehyde, the tributyl salt (1b) gave only a mixture of *Z*- and *E*-isomers of the stilbene (10) (85%); neither the styrene (11) nor the hydrolysis product (4) was detected in the crude reaction mixtures.



(1) a; R = Ph,
b; R = n - Bu



(2)



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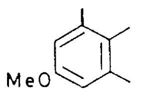

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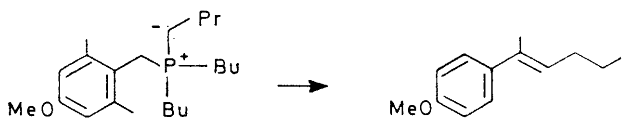
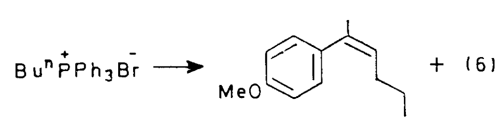


(5) (6)



(7)

Our studies suggested that only in those condensations involving the salt (1b) and aryl ketones should we expect

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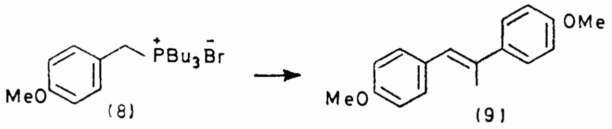
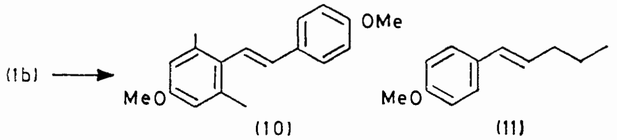
[1] For extensive bibliography since 1968 see S. Trippett, 'Ylides and Related Compounds' in 'Organophosphorus Chemistry,' vols. 1—6, *Chem. Soc. Specialist Periodical Reports*, 1970—1975; see also (*a*) A. Maercker, *Org. Reactions*, 1965, **14**, 270; (*b*) S. Trippett, *Quart. Rev.*, 1963, **17**, 406; (*c*) M. Schlosser, *Topics Stereochem.*, 1970, **5**, 1.

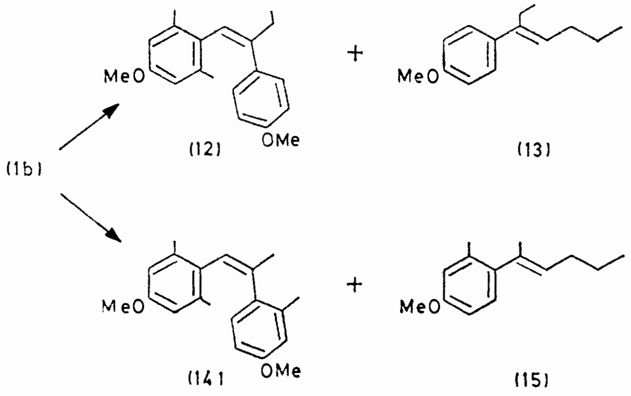
to observe products resulting from dichotomous ylide formation in (1b); this was confirmed in parallel studies.



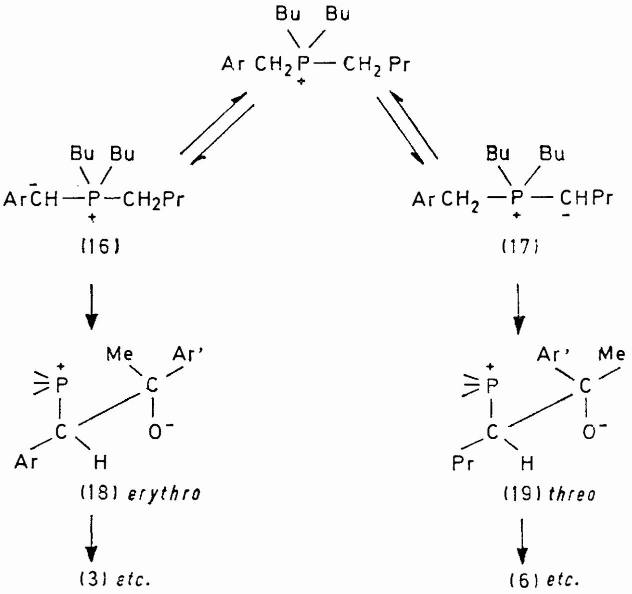


Condensations between (1b) and 4′-methoxypropiophenone and between (1b) and 4′-methoxy-2′-methylacetophenone both produced products [(12) + (13) and (14) + (15), respectively] resulting from dichotomous ylide formation. In both cases the hydrolysis product (4) was also obtained (32—40%). The configurations assigned to compounds (12)—(15), followed from inspection and comparison of spectral data with those of authentic *Z*- and *E*-stilbenes and styrenes (see Experimental section).

The stereospecificities of the reactions leading from (1b) to *Z*-stilbenes [(3), (12), and (14)] and *E*-styrenes [(6), (13), and (15)] are unprecedented. If we consider that C–C bond formation between the ylides (16) and (17) and the aryl alkyl ketones is the first step in both reactions, in one case (that leading to *Z*-stilbene) *erythro*-intermediate betaine formation [*viz.* (18)] must be invoked, whereas in the other (leading to *E*-styrene), *threo*-betaine formation [*viz.* (19)] has to occur (see Scheme 1); *syn*-elimination *via* the appropriate oxaphosphetan intermediates formed from the betaines then leads to *Z*-stilbene and *E*-styrene. Under otherwise identical conditions however, triphenylphosphonium butylide reacts with the same aryl alkyl ketones producing predominantly the corresponding *Z*-styrenes [(7) *etc.*; see Experimental section]. In addition, the triphenylphosphonium salt (1a) either produces *E*-stilbene [*viz.* (2)] † or does not react at all with the aryl ketones. In view of these comparative data it seems probable that the mechanisms which operate in these reactions are different from those in the reactions leading from the salt (1b) to compounds (3), (6), and (12)—(15).



An alternative explanation for the stereospecific reactions leading to compounds (3), (6), and (12)—(15) can be formulated, based on initial co-ordination of carbonyl oxygen to the phosphorus of the ylide (1b), leading to an oxyphosphorane intermediate (Scheme 2) (for discussion of this approach see ref. 2). Formation of this type of intermediate is plausible in the special case of (1b) and aryl alkyl ketones, because of the mutual inaccessibility of the carbon centres in the two reactants. Models suggest that this sequence could lead to an oxyphosphorane (20) which might equilibrate with a second oxyphosphorane (22) by intramolecular H exchange. With both aryl (Ar) and propyl (Pr) groups *anti* [see (21)] and Ar orientated in the least sterically crowded section of the equatorial plane, a rotational movement to the left about the $\overset{+}{\mathrm{C}}$–O bond would lead to the *erythro*-intermediate (23), whereas a rotational movement to the right would lead to the '*threo*'-intermediate (24); collapse of these intermediates by *syn*-elimination would then give rise to *Z*-stilbene and *E*-styrene, respectively.



SCHEME 1

EXPERIMENTAL

For general experimental details see ref. 3.

Tributyl-(4-methoxy-2,6-dimethylbenzyl)phosphonium Bromide (1b).—A solution of tributylphosphine (18 g) in dry benzene (100 ml) was added dropwise to a solution of

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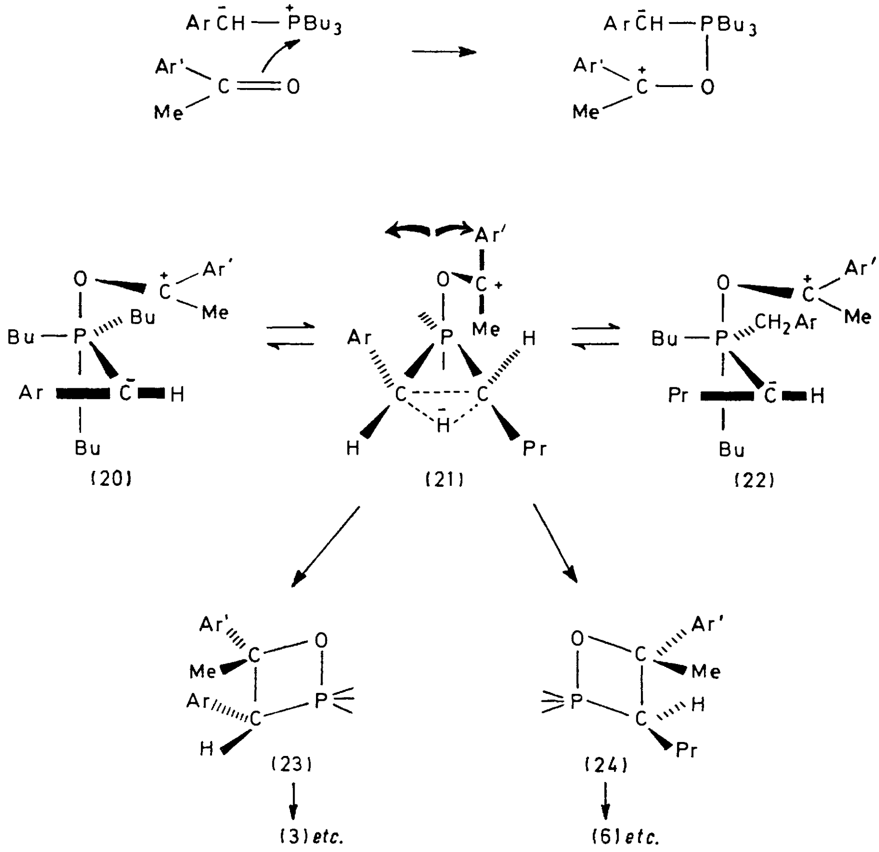
† In these reactions an *E*-stilbene could have resulted from stereomutation of a pre-formed *Z*-isomer during reaction (see Experimental conditions, preceding paper).

[2] W. P. Schneider, *Chem. Comm.*, 1969, **785**; see also E. Vedejs and K. A. J. Snoble, *J. Amer. Chem. Soc.*, 1973, **95**, 5778.

[3] B. G. James and G. Pattenden, *J.C.S. Perkin I*, 1974, **1195**.

4-methoxy-2,6-dimethylbenzyl bromide [from 4-methoxy-2,6-dimethylbenzyl alcohol (16.6 g)] in dry benzene (50 ml), and the mixture was then boiled under reflux for 2 h. The benzene was removed *in vacuo*, and the residual glass was then triturated with dry ether to give the *salt* (34.2 g, 90%), as a white powder, m.p. 124°, $\nu_{\text{max.}}$ (Nujol) 1 610, 1 585, 1 510, 1 250, 915, 840, and 735 cm^{-1}, τ 3.4 (2 H), 5.97 (d, *J* 15 Hz, $\mathrm{ArC}H_2\cdot\mathrm{P}^+$), 6.24 ($OCH_3$), 7.54br (s, 3 × $\mathrm{C}H_2\cdot\mathrm{CH_2}$), 7.6 (2 × ${:}\mathrm{CH\cdot CH_3}$), 8.55br (s, 3 × $\mathrm{CH_2\cdot C}H_2\cdot\mathrm{C}H_2\cdot\mathrm{CH_3}$), and 9.1 (t, *J* 7 Hz, $\mathrm{CH_2\cdot C}H_3$) (Found: C, 61.1; H, 9.7. $C_{22}H_{40}BrOP$ requires C, 61.3; H, 9.5%).



SCHEME 2

Reactions between Tributyl-(4-methoxy-2,6-dimethylbenzyl)-phosphonium Bromide and Aryl Ketones.—The reactions were carried out according to the general procedure described in the preceding paper. Products of reactions were separated by chromatography in benzene on silica gel.

(A) *With* 4'-*methoxyacetophenone*. Chromatography gave: (i) (E)-2-(4-*methoxyphenyl*)*hex*-2-*ene* (6) (0.28 g, 14%) (eluted first), $\lambda_{\text{max.}}$ 270 nm, $\nu_{\text{max.}}$ (film) 1 610, 1 575, 1 510, 1 250, 1 030, and 830 cm^{-1}, τ 2.7 (2 H, d, *J* 9 Hz), 3.2 (2 H, d, *J* 9 Hz), 4.32 (t, *J* 7 Hz, $\mathrm{C}H{:}\mathrm{CMe}$), 6.28 (OMe), 7.95 (q, *J* 7 Hz, $\mathrm{CH_2\cdot C}H_2\cdot\mathrm{CH}$), 8.03 (${:}\mathrm{CMe}$), 8.55 (sextet, *J* 7 Hz, $\mathrm{CH_2\cdot C}H_2\cdot\mathrm{CH_3}$), and 9.06 (t, *J* 7 Hz, $\mathrm{C}H_3\cdot\mathrm{CH_2}$) (Found: *m*/*e*, 190.1358, $C_{13}H_{18}O$ requires *M*, 190.1358); (ii) 3,4,5-trimethylanisole (4) (0.58 g, 37%) (eluted second) identical with an authentic sample; and (iii) (Z)-4,4'-*dimethoxy*-2,6,α'-*trimethylstilbene* (3) (0.85 g, 29%) (eluted third), which crystallised from ethanol as needles, m.p. 72°, $\lambda_{\text{max.}}$ (EtOH) 268 nm (8 700); $\nu_{\text{max.}}$ (Nujol) 1 608, 1 575, 1 515, 1 250, 860, 825, and 805 cm^{-1}, τ 3.08 (2 H, d, *J* 9 Hz), 3.40 (2 H, d, *J* 9 Hz), 3.53 (2 H), 3.72 (${C{:}CH}$), 6.32 (OCH_3), 6.35 (OCH_3), 7.79 (${:}\mathrm{C\cdot CH_3}$), and 7.98 (2 × ${:}\mathrm{CMe}$) (Found: C, 80.65; H, 7.9%; *m*/*e* 282. $C_{19}H_{22}O_2$ requires C, 80.8; H, 7.85%; *M*, 282). The stilbene was isomerised to the corresponding *E*-isomer with iodine in acetic acid (see preceding paper).

(B) *With* 4'-*methoxypropiophenone*. Chromatography gave: (i) (E)-3-(4-*methoxyphenyl*)*hept*-3-*ene* (13) (0.1 g, 5%) (eluted first), $\lambda_{\text{max.}}$ 252 nm; $\nu_{\text{max.}}$ (film) 1 610, 1 575, 1 510 1 250, 1 035, 830, and 800 cm^{-1}; τ 2.75 (2 H, d, *J* 9 Hz), 3.22 (2 H, d, *J* 9 Hz), 4.45 (t, *J* 7 Hz, ${:}\mathrm{C}H\cdot\mathrm{CH_2}$), 6.23 (OMe), 7.55 (q, *J* 7 Hz, ${:}\mathrm{C\cdot C}H_2\cdot\mathrm{CH_3}$), 7.85 (q, *J ca.* 7 Hz, ${:}\mathrm{CH\cdot C}H_2$ $\mathrm{CH_2}$), *ca.* 8.6 (m, $\mathrm{CH_2\cdot C}H_2\cdot\mathrm{CH_3}$), and 9.06 (t, 2 × $\mathrm{CH_2\cdot C}H_3$) (Found: *m*/*e*, 204.1514. $C_{14}H_{20}O$ requires *M* 204.1514); (ii) 3,4,5-trimethylanisole (0.59 g, 40%) (eluted second), identical with an authentic sample; and (iii) (Z)-α'-*ethyl*-4,4'-*dimethoxy*-2,6-*dimethylstilbene* (12) (0.9 g, 30%) (eluted third), which crystallised from aqueous ethanol as needles, m.p. 68°, $\lambda_{\text{max.}}$ (EtOH) 270 nm (10 950); $\nu_{\text{max.}}$ (Nujol) 1 603, 1 510, 1 250, 1 150, 850, and 835 cm^{-1}, τ 3.1 (2 H, d, *J* 9 Hz), 3.5 (2 H, d, *J* 9 Hz), 3.55 (2 H), 3.75 (olefinic ${:}\mathrm{CH}$), 6.3 (2 × OCH_3), 7.42 (q, *J* 8 Hz, $\mathrm{C}H_2\cdot\mathrm{CH_3}$), 7.97 (2 × aryl ${:}\mathrm{C\cdot CH_3}$), and 8.9 (t, *J* 8 Hz, $\mathrm{CH_2\cdot C}H_3$) (Found: C, 81.2; H, 8.2%; *m*/*e*, 296. $C_{20}H_{24}O_2$ requires C, 81.0; H, 8.2%; *M*, 296). The stilbene was isomerised to the corresponding *E*-isomer with iodine in acetic acid (see preceding paper).

(C) *With* 4'-*methoxy*-2'-*methylacetophenone*. Chromatography gave: (i) (E)-2-(4-*methoxy*-2-*methylphenyl*)*hex*-2-*ene* (15) (0.07 g, 3.5%) (eluted first), n_D^{23} 1.5160; $\lambda_{\text{max.}}$ (EtOH)

230 and 275 nm, $\nu_{max.}$ (film) 1 605, 1 570, 1 500, 1 235, 860, 840, and 800 cm^{-1}; τ 3.07 (d, *J* 9 Hz, aryl :CH), 3.34 (aryl :CH), 3.48 (d, *J* 9 Hz, aryl :CH), 4.76 (t, *J* 8 Hz, C:CH), 6.28 (OCH_3), 7.78 (aryl :C·CH_3), 7.88 (q, *J* 8 Hz, C:CH·C*H*$_2$·CH_2), 8.13 (olefinic CH_3), 8.56 (sextet, *J* 8 Hz, CH_2·C*H*$_2$·CH_3), and 9.05 (t, *J* 8 Hz, CH_2·C*H*$_3$) (Found: *m/e*, 204.1514. $C_{14}H_{20}O$ requires *M*, 204.1514); (ii) 3,4,5-trimethylanisole (0.48 g, 32%) (eluted second), identical with an authentic sample; and (iii) (Z)-4,4'-*dimethoxy*-2,2',6,α'-*tetramethylstilbene* (14) (0.3 g, 10%), an oil, $\lambda_{max.}$ 231 and 280 nm; $\nu_{max.}$ (film) 1 610, 1 575, 1 500, 1 260, 1 190, 1 160, and 835 cm^{-1}; τ 3.23 (d, *J* 9 Hz, aryl :CH), 3.4—3.7 (m, 4 × aryl :C*H* plus 1 × olefinic :CH), 6.4 (2 × OCH_3), 7.85 (olefinic :C·CH_3), and 7.96 (3 × aryl :C·CH_3), *m/e* 296 ($C_{20}H_{24}O_2$). The stilbene was isomerised to the *E*-isomer with iodine in acetic acid (see preceding paper).

(D) Reaction with *p*-anisaldehyde, followed by chromatography on silica gel [benzene–ethyl acetate (97 : 3)] gave a 1 : 9 mixture (85%) of *Z*- and *E*-isomers of 4,4-dimethoxy-2,6-dimethylstilbene (10). Crystallisation gave the *E*-isomer, m.p. 82—83°, identical with an authentic sample.

(Z)-2-(4-*Methoxyphenyl*)*hex*-2-*ene* (7).—By the general procedure, butyltriphenylphosphonium bromide and 4'-methoxyacetophenone produced a 9 : 1 mixture of *Z*- and *E*-isomers of the alkene. Chromatography in benzene on silica gel gave: (i) the (Z)-*alkene* (eluted first) (70%), τ 2.93 (2 H, d, *J* 9 Hz), 3.2 (2 H, d, *J* 9 Hz), 4.6 (t, *J* 7 Hz, :C*H*·CH_2), 6.28 (OMe), 8.05 (q, *J* 7 Hz, :CH·C*H*$_2$·CH_2), 8.02 (:CMe), 8.62 (sextet, *J* 7 Hz, CH_2·C*H*$_2$·CH_3), and 9.18 (t, *J* 7 Hz, CH_2·C*H*$_3$) (Found: *m/e*, 190.1358. $C_{13}H_{18}O$ requires *M*, 190.1358); and (ii) the *E*-alkene (eluted second) (10%), identical with an authentic sample.

(Z)-3-(4-*Methoxyphenyl*)*hept*-3-*ene*.—By the general procedure, butyltriphenylphosphonium bromide and 4'-methoxypropiophenone produced a 9 : 1 mixture of *Z*- and *E*-isomers of the alkene. Chromatography in benzene on silica gel gave: (i) the (Z)-*alkene* (eluted first) (65%), τ 2.96 (2 H, d, *J* 9 Hz), 3.20 (2 H, d, *J* 9 Hz), 4.63 (t, *J* 7 Hz, :C*H*·CH_2), 6.26 (OMe), 7.69 (q, *J* 7 Hz, :C·C*H*$_2$·CH_3), 8.09 (q, *J* 7 Hz, :CH·C*H*$_2$·CH_2), 8.69 (sextet, *J* 7 Hz, CH_2·C*H*$_2$·CH_3), 9.06 (t, *J* 7 Hz, :C·CH_2·C*H*$_3$), and 9.18 (t, *J* 7 Hz, CH_2·C*H*$_3$) (Found: *m/e*, 204.1514. $C_{14}H_{20}O$ requires *M*, 204.1514); and (ii) the (*E*)-alkene (eluted second) (6%), identical with an authentic sample.

Tributyl-(4-*methoxybenzyl*)*phosphonium Bromide* (8).—The *salt*, prepared from *p*-anisyl alcohol *via* the corresponding bromide in the usual manner, had m.p. 62—63°, $\nu_{max.}$ (Nujol) 1 605, 1 580, and 1 510 cm^{-1}, τ 2.14 (2 H, d, *J* 9 Hz), 2.58 (2 H, d, *J* 9 Hz), 5.59 (d, *J* 14 Hz, ArC*H*$_2$·P^+), 6.2 (OMe), 7.4—7.7 (m, 3 × P^+·CH_2), 8.4—8.6 (12 H, m), and 9.05 (t, *J* 7 Hz, 3 × CH_2·C*H*$_3$) (Found: C, 59.8; H, 10.1. $C_{20}H_{36}BrOP$ requires C, 59.6; H, 8.9%).

(E)-4,4'-*Dimethoxy*-α-*methylstilbene* (9).—By the general procedure (see preceding paper), tributyl-(4-methoxybenzyl)phosphonium bromide and acetophenone gave the stilbene (60%), m.p. 122—123° (from glacial acetic acid) (lit.,[4] 124°), τ 2.55 (2 H, d, *J* 8 Hz), 2.71 (2 H, d, *J* 8 Hz), 3.11 (4 H, d, *J* 8 Hz), 3.3 (:CH), 6.2 (OMe), and 7.75 (:CMe), *m/e* 254.

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[4] R. L. Huang, *J. Chem. Soc.*, 1954, 2539.