Efficient Wittig–Horner Synthesis of Acyclic α-Enones with an Asymmetric Carbon at the γ-Position Using Barium Hydroxide

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β-Monosubstituted acylic α-enones with an asymmetric carbon at the γ-position: (E)-$(5RS)$-5-phenylhex-3-en-2-one, (**4a**), (E)-$(6RS)$-2,2-dimethyl-6-phenylhept-4-en-3-one, (**4b**), (E)-$(4RS)$-1,4-diphenylpent-2-en-1-one, (**4c**), (E)-$(5RS)$-6,6-dimethyl-5-phenylhept-3-en-2-one, (**4d**), (E)-$(6RS)$-2,2,7,7-tetramethyl-6-phenyloct-4-en-3-one, (**4e**), and (E)-$(4RS)$-5,5-dimethyl-1,4-diphenylhex-2-en-1-one, (**4f**), have been prepared by Wittig–Horner reaction of aliphatic aldehydes and 2-oxoalkylphosphonates with different degrees of steric hindrance. The use of activated barium hydroxide C-200 as the base in 1,4-dioxane provided an efficient and stereoselective synthetic method, remarkably free of competing side-reactions. The reaction course was found to depend on the phosphonate acidity: triethyl phosphonoacetate reacts through an interfacial solid–liquid mechanism, while the more acidic 2-oxoalkylphosphonates dissolve the barium hydroxide and the reaction takes place in the homogeneous phase probably due to a phase-transfer-like mechanism. The anionic species formed from the 2-oxoalkylphosphonates by the action of barium hydroxide C-200 in 1,4-dioxane were detected by ^{31}P n.m.r. spectroscopy. The α-enones (**4**) are useful model compounds for the study of diastereofacial selectivity in nucleophilic addition reactions.
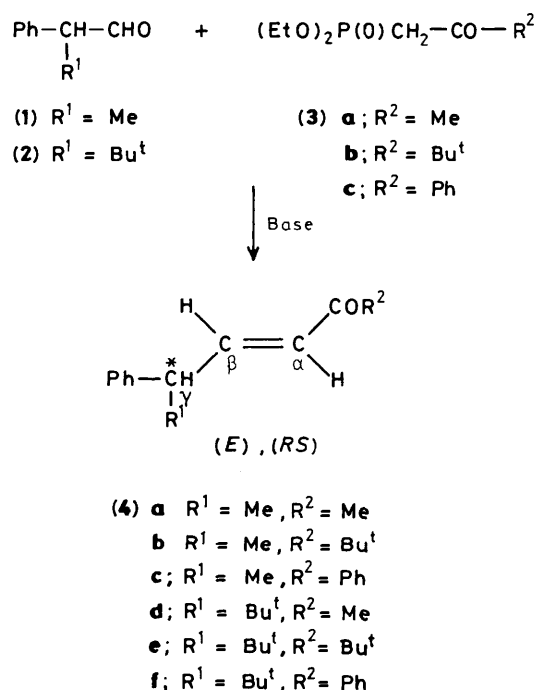
The Wittig and Wittig–Horner olefination reactions of aldehyde and ketone functionalities are versatile methods for the preparation of unsaturated compounds.[1-3] These processes have become widely recognized and applied due to (i) the ease of obtaining carbon–carbon double bonds in a predictable position and (ii) the possibility of stereochemical control. Although a considerable deal of work has been done on their mechanistic and synthetic aspects, intermediate mechanistic details remain to be elucidated.[4-13]

In the last few years the Wittig–Horner reaction has been carried out using two-phase liquid–liquid [6,7] or solid–liquid [8-13] conditions and better yields are generally obtained than those achieved in the homogeneous phase. However, undesired side-reactions of both the starting materials (crotonization, Cannizzaro reaction, etc.) and products (double bond shifts, etc.) often cannot be avoided.[5a,6,7,9,11]

Recently, a family of activated barium hydroxide catalysts with different microcrystalline structures has been described.[14,15] Under interfacial solid–liquid conditions, the microcrystalline structure of the solid determines the nature of the active sites (their geometrical, steric and electrostatic properties) and, therefore the mechanism of the organic reactions.[12,15-17] Thus, microcrystalline barium hydroxide C-200 [Ba(OH)$_2$·0.8H$_2$O] is a very active catalyst for the carbanionic process under interfacial solid–liquid conditions such as aldol condensation,[15] Michael addition,[16] Claisen–Schmidt condensation,[17] and the Wittig–Horner reaction with triethyl phosphonoacetate and diethyl cyanomethylphosphonate.[12a]

In a preliminary communication [18] an improved synthesis of α,β-unsaturated ketones by Wittig–Horner reaction using barium hydroxide C-200 was reported and an interfacial solid–liquid mechanism was postulated taking into account studies on the Wittig–Horner synthesis of acrylates.[12] Nevertheless, some new facts which are not in agreement with this assumption for the Wittig–Horner synthesis of α-enones have been found. In

order to obtain a general view of the activity of barium hydroxide C-200 in the Wittig–Horner reaction we now describe our studies on the reaction of 2-oxoalkylphosphonates and aliphatic aldehydes with different degrees of steric hindrance (Scheme 1). The influence of the acidity of

$$Ph-\underset{\underset{R^1}{|}}{CH}-CHO \quad + \quad (EtO)_2P(O)\,CH_2-CO-R^2$$

(1) R^1 = Me

(2) R^1 = Bu^t

(3) **a** ; R^2 = Me

b ; R^2 = Bu^t

c ; R^2 = Ph

Base ↓

$$Ph-\underset{\underset{R^1}{\overset{\gamma}{|}}}{\overset{*}{CH}}\underset{\beta}{\diagdown}C=C\underset{\alpha}{\diagup}\overset{\diagup COR^2}{\diagdown H} \quad \diagup H$$

(E) , (RS)

(**4**) **a** R^1 = Me , R^2 = Me

b R^1 = Me , R^2 = Bu^t

c ; R^1 = Me , R^2 = Ph

d ; R^1 = Bu^t, R^2 = Me

e ; R^1 = Bu^t, R^2 = Bu^t

f ; R^1 = Bu^t, R^2 = Ph

Scheme 1. Efficient Wittig–Horner synthesis of acyclic α-enones with an asymmetric carbon at the γ-position using barium hydroxide.

Table 1. Wittig–Horner reactions of 2-oxoakylphosphonates (3) and aldehydes (1) and (2) with activated barium hydroxide C-200 and sodium hydride.

Entry	Aldehyde R^1	2-Oxoalkylphosphonate R^2	Reaction conditions			α-Enone	Yield (%)[b]
			Method[a]	Time	$T/°C$		
1	Me	Me	A	10 min	70	(4a)	96
2	Me	Me	B	3 h	25	(4a)	90
3	Me	Bu^t	A	10 min	70	(4b)	98
4	Me	Bu^t	B	3 h	25	(4b)	91[c]
5	Me	Ph	A	10 min	70	(4c)	84
6	Me	Ph	B	3 h	25	(4c)	75
7	Bu^t	Me	A	15 min	70	(4d)	96
8	Bu^t	Me	B	3 h	40	(4d)	94
9	Bu^t	Bu^t	A	15 min	70	(4e)	96
10	Bu^t	Bu^t	B	3 h	25	(4e)	67
11	Bu^t	Bu^t	B	3 h	40	(4e)	94
12	Bu^t	Ph	A	15 min	70	(4f)	96
13	Bu^t	Ph	B	4 h	40	(4f)	95

> Method A: Activated barium hydroxide C-200 in 1,4-dioxane, molar ratio base:aldehyde, 0.52. Method B: NaH in DME, molar ratio base:aldehyde, 1.0. [b] Determined by gas chromatography ($\pm 2\%$). [c] Deduced by ^{1}H n.m.r spectroscopy.

phosphonate on the course of the reaction is discussed. ^{31}P N.m.r. spectroscopy was applied to detect the anionic species formed from 2-oxoalkylphosphonates, (3), by the action of the activated barium hydroxide C-200 in 1,4-dioxane.[5] The effectiveness of barium hydroxide C-200 was compared with that of other bases: NaH, K_2CO_3, Cs_2CO_3, and KF–Al$_2$O$_3$.

The synthetic method has been directed towards the preparation of six β-monosubstituted acyclic α-enones (4a–f) with an asymmetric carbon at the γ-position, useful model compounds for the study of diastereofacial selectivity in nucleophilic addition reactions.[19] The α-enones (4d–f) are novel and (4b) and (4c) have only been reported in connection with stereoselection studies.[19b] The synthesis of these α-enones is achieved, in this way, for the first time.

Results and Discussion

The Wittig–Horner reaction of aliphatic aldehydes ($\pm$)-2-phenylpropanal **(1)** and ($\pm$)-3,3-dimethyl-2-phenylbutanal **(2)** with the 2-oxoalkylphosphonates (3) (Scheme 1) was carried out using activated barium hydroxide C-200 in 1,4-dioxane (method A) and sodium hydride (NaH) in 1,2-dimethoxyethane (DME) ^{20,21} (method B). The results obtained are shown in Table 1. The stereochemistry of the α-enones (4) was the same in all cases; only the (E)-(RS)-isomer was obtained. The (Z)-(RS) isomer and/or other by-products were not detectable in yields higher than 2% (experimental error of the analytical method).

The process is strongly influenced by the reaction temperature when strong base such as NaH in anhydrous medium (method B) is used. ($\pm$)-3,3-Dimethyl-2-phenylbutanal (2), exhibits lower reactivity than ($\pm$)-2-phenylpropanal (1), in these conditions and higher reaction temperature must be employed in the former case to obtain similar yields (Table 1, entries 4, 10, and 11). This fact can be explained by the steric hindrance effect of the group in the α-position to the CHO (Bu^t versus Me).

α-Enones (4) can readily undergo double bond shifts under basic conditions due to the presence of a benzylic hydrogen atom (γ-H).^{5a,7a,9} We have observed this isomerization in the case of α-enones (4a–c), using the NaH–DME system at reaction temperatures over 25 °C. Thus, (E)-(RS) 2,2-dimethyl-6-phenylhept-4-en-3-one (4b), was partially transformed into a mixture of the (E)- and (Z)-isomers of 2,2-dimethyl-6-phenylhept-5-en-3-one (5), in the presence of NaH at 40 °C

(Scheme 2). Nevertheless, such a side-reaction was not observed for the α-enones (4d–f), probably due to the presence of a bulkier substituent at the γ-position (Bu^t versus Me) which diminishes the stabilization of the β,γ-unsaturated system by
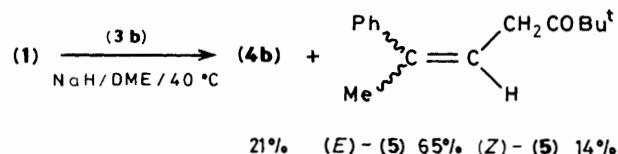
Scheme 2. Efficient Wittig–Horner synthesis of acyclic α-enones with an asymmetric carbon at the γ-position.

steric inhibition of the conjugation between the C_β=C_γ bond and the γ-Ph group.^{22} So the process with (1) must be performed at 25 °C, and with (2) at 40 °C for the optimum yield (Table 1).

Activated barium hydroxide C-200 in 1,4-dioxane led to better results at 70 °C (method A). The experimental procedure is cheap and easier than method B (anhydrous medium and inert atmosphere are avoided). Lower molar ratios of base:aldehyde (0.52 versus 1.0) and reaction times are necessary to obtain similar yields (Table 1). Furthermore, steric hindrance of groups R^1 and R^2 does not affect the conversion, and no side-reactions were observed under the experimental conditions employed.

The scope of the catalytic activity of barium hydroxide C-200 in the Wittig–Horner reaction with triethyl phosphonoacetate has been treated previously.^{12} The process has proved to be a surface reaction^{12} and the structure of the adsorbed species on the surface of the catalyst has been proposed.^{12b,c} In the present work the preparation of α-enones has been accomplished using the same experimental conditions and in general, shorter reaction times than necessary for acrylate synthesis.^{12a} The increase in yield by the addition of a small amount of water shown in the acrylate synthesis^{12} was only detected in the synthesis of α-enones at low reaction temperatures (Table 2, entries 2, 3, 4, and 5). Although these discrepancies may be justified on the basis of the proposed interfacial solid–liquid mechanism as a consequence of the higher acidity of the methylene protons in the 2-oxoalkylphosphonates than in the triethyl phosphonoacetate,^{1,7a} the following observations in the reaction of (1) and (3a) suggest a more essential influence of the nature of the phosphonate on the course of the reaction.

Table 2. Wittig–Horner reaction of (1) with (3a) under different experimental conditions.

Entry	Catalyst	Molar ratio catalyst: (1)	Solvent[a]	T/°C	Time	Yield (%) of (4a)[b]
1	C-200	0.52	1,4-Dioxane	70	5 min	50
2	C-200	0.52	1,4-Dioxane	70	10 min	96
3	C-200	0.52	1,4-Dioxane (without H_2O)	70	10 min	95
4	C-200	0.52	1,4-Dioxane	30	10 min	78
5	C-200	0.52	1,4-Dioxane (without H_2O)	30	10 min	45
6	C-200–TBMPHE[c]	0.52	1,4-Dioxane	70	10 min	95
7	C-200–BA[c]	0.52	1,4-Dioxane	70	10 min	95
8	K_2CO_3	1.50	1,4-Dioxane	70	25 min	74
9	Cs_2CO_3	1.28	1,4-Dioxane	70	25 min	95
10	$KF–Al_2O_3$	d	d	25	22 h	50

[a] The reactions were carried out in a lightly hydrated medium except for specified cases. [b] Determined by gas chromatography ($\pm 2\%$). [c] The activated barium hydroxide was poisoned (ref. 14) by 2,6-di-t-butyl-4-methylphenol (TBMPHE) and benzoic acid (BA) for these experiments. [d] The reaction was carried out without organic solvent, using 1.25 g of $KF–Al_2O_3$(B), 2.5 mmol of (3a), 2.5 mmol of (1), and 0.5 g of water (ref. 11).

Selective poisoning experiments [14] of the strongly basic sites ($pK_a > 11.7$) by 2,6-di-t-butyl-4-methylphenol (TBMPHE) ($pK_a = 11.7$) and one of the weakly and strongly basic sites ($pK_a > 4.2$) by benzoic acid (BA) ($pK_a = 4.2$) of the activated barium hydroxide C-200 does not influence the process (Table 2, entries 6 and 7) while the strong basic sites ($pK_a > 11.7$) are mainly responsible for the catalytic activity in the Wittig–Horner reaction with triethyl phosphonoacetate.[12c] On the other hand, when the adsorptions of the 2-oxoalkylphosphonates (3) on activated barium hydroxide C-200 were attempted, following the method previously described in the literature,[12b,c] the solid was practically dissolved. Similar behaviour was observed in the case of acetylacetone[23] and may be related to the acidity of the organic compound. Triethyl phosphonoacetate and acetylacetone exhibit pK_a values of 12.2[24] and 9.0,[23] respectively, while the pK_a of the more acidic 2-oxoalkyl-phosphonates (3), may be lower and similar to that of $Ph_3P^+-CH_2CO-Ph$ for which a value of 5.6 has been reported.[25] Therefore, it seems that those compounds with $pK_a < 11$ produce total or partial dissolution of solid barium hydroxide C-200 and therefore the reactions should not be sensitive to the structure of the solid and to the selective poisoning experiments of the active sites. In these cases, the reaction intermediates should be produced in the solid phase by direct reaction with the OH^- of the barium hydroxide C-200 lattice and go to the liquid phase. Thus, the process should take place in the homogeneous phase through a phase-transfer-like mechanism. The intermediates produced from the 2-oxoalkylphosphonates (3), by means of the activated barium hydroxide C-200 must be complex anionic species with a structure probably similar to those described by Seyden-Penne and his co-workers[26] for the anionic species formed from methyl diethyl phosphonoacetate by the action of lithium bases in tetrahydrofuran.

To gather more evidence for the above assumptions, [31]P n.m.r. spectra of the filtered solutions prepared from 2-oxoalkylphosphonates (3), by the action of barium hydroxide C-200 in 1,4-dioxane in the reaction conditions [molar ratio C-200:(3a) = 0.52; 1% water; 70 °C; 10 min] were recorded at 32.2 MHz and compared with those of the corresponding 2-oxoalkylphosphonates recorded under the same conditions. In all cases, only a broad singlet was observed and the ^{31}P signal appears shifted to low-field with respect to the 2-oxoalkyl-phosphonate [$\Delta\delta$ (3a) 10.3, (3b) 14.3, (3c) 13.0 p.p.m.]. These ^{31}P downfield shifts are in agreement with literature data[5a,26] and confirm the presence of the anionic species in the liquid phase where the positive charge of phosphorus is increased by the presence of an interaction $P\rightarrow O:\rightarrow$empty orbitals to cation Ba^{II}.

Two proofs were performed using filtered solutions of the anionic species prepared as above from (3a), under the same reaction conditions (70 °C, 10 min). First, the reaction with aldehyde (1) was carried out leading to the corresponding α-enone (4a) in high yield. Thus, the anionic species formed in the 1,4-dioxane solution are really the anionic reactive species and the process must take place in the homogeneous phase. Also, the reaction was achieved with an equimolar mixture of (1) and (3a), the reaction mixture was filtered and the [31]P n.m.r. spectrum of the clear solution obtained only exhibited the signal of (3a) but not that of the corresponding anionic species. Thus, it seems that the anionic species is not a catalyst and the process is not reversible under these conditions.

The synthesis of (E)-(RS)-5-phenylhex-3-en-2-one (4a), was used to compare the effectiveness of the activated barium hydroxide C-200 with other bases: K_2CO_3,[4c,10] Cs_2CO_3,[4c,10] and $KF–Al_2O_3$.[11,27] In any case, secondary reactions were detected, but barium hydroxide C-200 led to better or similar yields using lower molar ratios base:aldehyde and/or reaction times (Table 2, entries 2, 4, 8, 9, and 10). Furthermore, the yield in the α-enone (4a) is higher at lower reaction times than those reported in the literature by other synthetic methods.[19a,28]

Therefore the use of barium hydroxide C-200 in the Wittig–Horner reaction provides an efficient and highly stereoselective method for the preparation of acyclic α-enones remarkably free from side-reactions. The process takes place through an interfacial solid–liquid mechanism in the acrylate synthesis[12] and in the homogeneous phase probably by a phase-transfer-like mechanism in the synthesis of α-enones. The change of the pathway seems to be related to the acidity of the phosphonate.

The structural study of the α-enones (4a–f) has been carried out by ^{1}H and [13]C n.m.r. spectroscopy. The proton magnetic parameters and the carbon chemical shifts deduced from the analysis of the spectra are collected in Tables 3 and 4.

The more significant parameters for the configurational and conformational study are the proton vicinal coupling constants, $^3J_{\alpha\beta}$ and $^3J_{\beta\gamma}$, and the allylic coupling constant, $^4J_{\alpha\gamma}$. The assignment of the (E) configuration to the carbon–carbon double bond of the α-enones (4a–f) was unmistakably achieved on the basis of the values of vicinal coupling constants for alkenic protons, $^3J_{\alpha\beta}$. This coupling constant exhibits a value of 15.4 $\pm$ 0.5 Hz in all cases, in agreement with a trans disposition between α-H and β-H protons.[29]

The experimental values of the allylic coupling constants, $|^4J_{\alpha\gamma}|$ [$\simeq 1.2$ Hz for (4a–c) and ≤ 0.6 Hz for (4d–f)] and the vicinal coupling constants $^3J_{\beta\gamma}$ [6.5 $\pm$ 0.3 Hz for (4a–c)] and $\simeq$ 10.0 Hz for (4d–f) indicated a notable difference in the conformational equilibria about the rotational system $C_\beta–C_\gamma$ of these two series of α-enones (4a–c) and (4d–f). Taking into account the relation between the value of $^4J_{\alpha\gamma}$ and the dihedral

**Table 3.** Proton magnetic parameters of α-enones (4a–f) (CDCl$_3$).

Magnetic parameters	(4a)	(4b)	(4c)	(4d)	(4e)	(4f)
Chemical shifts δ (p.p.m.)[a]						
γ-H[b]	3.61	3.59	3.69	3.13	3.15	3.27
α-H (dd)	6.01	6.41	6.82	6.03	6.43	6.89[c]
β-H (dd)	6.88	7.05	7.14	7.18	7.35	7.49
γ-H (m)	7.12–7.27	7.18–7.40	7.21–7.90	7.10–7.20	7.17[d]	7.18–7.90
R^1	2.21(s)	1.13(s)	7.21–7.90	2.19(s)	1.10(s)	7.18–7.90
R^2	1.43(d)	1.41(d)	1.47(d)	0.90(s)	0.90(s)	0.94(s)
Coupling constants J/Hz						
$^3J_{\alpha\beta}$	16.0	15.3	15.5	15.6	14.9	15.2
$|^4J_{\alpha\gamma}|$	1.3	1.2	1.0	0.6	0.5	–[c]
$^3J_{\beta\gamma}$	6.6	6.8	6.3	9.9	10.0	10.0
$^3J_{\gamma\text{-}R^2}$	7.0	7.1	7.0	—	—	—

[a] Abbreviations: (d) doublet, (dd) doublet of doublets, (m) multiplet, and (s) singlet. [b] This signal appears as an apparent quadruplet and an apparent doublet for α-enones (4a–c) and (4d–f), respectively. [c] This signal appears as an apparent doublet and the corresponding allylic coupling constant could not be determined. [d] Apparent singlet.

Table 4. ^{13}C Chemical shifts of α-enones (4a–f) (CDCl$_3$).

δ (p.p.m.)	(4a)	(4b)	(4c)	(4d)	(4e)	(4f)
γ-C	42.26	42.28	42.53	59.99	60.06	60.27
α-C	129.75	122.80	124.55	132.29	125.81	126.60
β-C	151.45	150.66	152.93	147.45	146.98	149.31
γ-Ph; para-C	126.86	126.58	126.71	126.71	126.54	127.15
ortho-C	127.35	127.24	127.32	129.18	129.32	129.24
meta-C	128.82	128.60	128.46[a]	128.12	127.98	128.04[a]
ipso-C	143.48	143.72	143.43	140.81	141.10	140.82
CO	198.40	204.15	190.95	197.75	203.76	190.21
R^1	26.95	26.15	128.46[b]	27.35	26.18	128.04[b]
		42.93	128.68[a,b]		42.78	128.45[a,b]
			132.56 para-C			132.59 para-C
			137.98 ipso-C			137.93 ipso-C
R^2	20.25	20.63	20.42	28.04	28.07	28.04
				34.57	34.57	34.66

[a] Interchangeable assignments. [b] These signals correspond to ortho-C and/or meta-C of the PhCO group.

(a)

(4d–f)   (b)
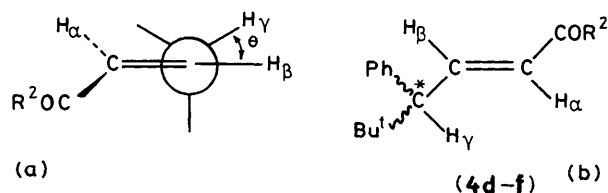
Figure 1. Efficient Wittig–Horner synthesis of acyclic α-enones with an asymmetric carbon at the γ-position

angle between the plane of the double bond and the adjacent C$_\gamma$–H$_\gamma$ bond [29a] [Figure 1(a)], the α-enones (4d–f); R^1 = Bu^t), with a small value of $|^4J_{\alpha\gamma}|$ can be considered practically monoconformational, adopting a preferred conformation with γ-H and the plane of the double bond eclipsed [29a,30] [Figure 1(b)]. The observed value of $^3J_{\beta\gamma} \simeq$ 10.0 Hz are in agreement with an anti arrangement of β-H and γ-H protons [29] and confirm this assumption. However, the α-enones (4a–c; R^1=Me), that have a high value of $|^4J_{\alpha\gamma}|$ and an averaged value of $^3J_{\beta\gamma}$ should be described as a conformational mixture of rotamers about the C$_\beta$–C$_\gamma$ bond.

The new α-enones (4d–f) are proposed as better model compounds than (4a–c) for stereoselection studies owing to their higher stability towards isomerization and their mono-conformational character with respect to rotation around the C$_\beta$–C$_\gamma$ bond.

Experimental

M.p.s were measured on a Büchi SMP-20 apparatus and are uncorrected. G.l.c. analyses were performed on a Perkin-Elmer Sigma-3 instrument provided with a flame ionization detector and a Sigma-10 data collector. The column used (1/4 in × 0.90 m) was a 10% BDS on Chromosorb W-AW-DMCS. I.r. spectra were measured as CHCl$_3$ solutions in NaCl cells on a Perkin-Elmer 599B spectrophotometer. Mass spectra were recorded on a Hewlett–Packard 5993 mass spectrometer. ^{1}H, ^{13}C, and ^{31}P n.m.r. spectra were recorded on a Varian FT-80A(PFT) spectrometer at 303 K. The recording conditions were: ^{1}H n.m.r. (79.542 MHz), 13% w/v CDCl$_3$ solutions with Me$_4$Si as the internal reference, acquisition time 2.047 s, spectral width 800 Hz and pulse width 7 μs; ^{13}C n.m.r. (20 MHz), three types of spectra, proton noise-decoupled (to determine the chemical shifts), off-resonance decoupled and proton-coupled spectra (to help assign the signals) were recorded using 25% w/v CDCl$_3$ solutions with Me$_4$Si as the internal reference, acquisition time 1.638 s, delay time 1.64 s, spectral width 5 000 Hz and pulse width 5 μs (for proton-coupled spectra gated decoupling, with the decoupler on during delay, was employed); ^{31}P n.m.r. (32.2 MHz, broad band proton decoupling mode), 1,4-dioxane solutions with a capillary filled with P(OMe)$_3$ as internal reference and external lock, acquisition time 1.638 s, spectral width 5000 Hz and pulse width 5 μs, chemical shifts are refer-enced against external 85% phosphoric acid and positive δ values are in the direction of increasing frequency.[26,31]

Tetrahydrofuran (THF) and benzene were purified in the usual manner and distilled from LiAlH$_4$ and sodium, respectively. 1,2-Dimethoxyethane (DME) and 1,4-dioxane were distilled over LiAlH$_4$ and sodium, respectively. Barium hydroxide C-200 was prepared as described previously[32] and activated prior to use in the reaction flask by being heated at 140 °C for 1 h under N$_2$ flow. The number of basic sites was described previously.[14] The selective poisoning experiments of the basic sites by 2,6-di-t-butyl-4-methylphenol (TBMPHE), and benzoic acid (BA), were achieved following the procedure reported in the literature.[14] Potassium fluoride supported on alumina [KF/Al$_2$O$_3$(B)] was prepared by the method described by Texier–Boullet et al.[11] Potassium carbonate and caesium carbonate were commercial products (Fluka).

Diethyl 2-oxopropylphosphonate (3a), diethyl 3,3-dimethyl-2-oxobutylphosphonate (3b), and diethyl 2-oxo-2-phenylethylphosphonate (3c) were prepared and purified following the method described by Mathey et al.[33] (±)2-Phenylpropanal (1) a commercial product, was obtained from Merck. (±)-3,3-Dimethyl-2-phenylbutanal (2), was obtained by an improved modification of the method followed by Lodge and Heathcock[34] from 2,2-dimethyl-1-phenylpropanone[35] via an epoxide. Thus, (±)-2-(1,1-dimethylethyl)-2-phenyloxirane[34] was prepared in a yield of 93% (versus 60%[34]) from 2,2-dimethyl-1-phenylpropanone and trimethylsulphonium iodide using a greater molar ratio NaH:trimethylsulphonium iodide (2.0 versus 1.0). The product exhibited a chromatographic purity of 98% without purification. Furthermore, the epoxide was directly transformed into the aldehyde (2), by acidic rearrangement.[36]

(±)-3,3-Dimethyl-2-phenylbutanal (2). BF$_3$·Et$_2$O (10.4 g, 73 mmol) was added drop wise to a solution of (±)-2-(1,1-dimethylethyl)-2-phenyloxirane (2.5 g, 14 mmol)[34] in dry benzene (115 cm^3) at room temperature. The mixture was stirred at this temperature for 30 min and diluted with water. The organic layer was separated and the aqueous phase was extracted with ether (3 × 100 cm^3). The organic phase was washed with water, dried (MgSO$_4$), and concentrated to leave (2) (2.0 g, 80%) with 92% g.l.c. purity.

Typical Procedure for Wittig–Horner Reactions.—Method A. A mixture of activated barium hydroxide C-200 (0.250 g, 1.30 mmol), 2-oxoalkylphosphonate (3) (2.5 mmol), and 1,4-dioxane (6 cm^3) was stirred at the reaction temperature (Tables 1 and 2) for 10 min in order to produce the anionic species. The mixture turned yellow, white, or orange from (3a), (3b), and (3c), respectively. A solution of (1) or (2) (2.5 mmol) in 1,4-dioxane (2 cm^3) with water (0.05 ml) was then added and the reaction mixture stirred at the same temperature for the reaction time (Tables 1 and 2). Addition of 10% aqueous HCl was continued till acidic pH and the mixture was filtered. The organic layer was separated and the aqueous phase extracted with ether (3 × 30 cm^3). The organic layer was washed with water and saturated aqueous sodium hydrogen carbonate, dried (MgSO$_4$), and the solvent evaporated to yield the crude product mixture.

Method B. A solution of 2-oxoalkylphosphonate (3) (10 mmol) in dry DME (6 cm^3) was added to a stirred suspension of 80% sodium hydride (Merck, in paraffin oil) (0.288 g, 10 mmol) in dry DME (20 ml) at 10–15 °C under N$_2$. The mixture was refluxed for 15 min, cooled to 15 °C, and then a solution of (1) or (2) (10 mmol) in dry DME (6 cm^3) was added. The mixture was stirred at 25 °C (or 40 °C) for the reaction times (Table 1) and quenched with water. The organic layer was separated and the aqueous phase extracted with ether (3 × 50 cm^3). The organic layer was washed with water and saturated aqueous sodium hydrogen carbonate, dried (MgSO$_4$), and concentrated to yield the crude product mixture.

Reactions using M$_2$CO$_3$.—A mixture of solid carbonate, phosphonate (3a), aldehyde (1), 1,4-dioxane, and water was stirred at 70 °C for 25 min. The reaction was then quenched with 10% aqueous HCl and worked up as described in method B. The following quantities were used: K$_2$CO$_3$ (0.414 g, 3 mmol), (3a) (0.485 g, 2.5 mmol), (1) (0.268 g, 2.0 mmol), 1,4-dioxane (5 cm^3) and water (0.05 cm^3); Cs$_2$CO$_3$ (0.880 g, 2.7 mmol), (3a) (0.524 g, 2.7 mmol), (1) (0.281 g, 2.1 mmol), 1,4-dioxane (5 cm^3), and water (0.05 cm^3).

Reaction with Potassium Fluoride–Alumina.—KF–Al$_2$O$_3$(B)[11] (1.25 g) was added to a mixture of (3a) (0.485 g, 2.5 mmol), (1) (0.335 g, 2.5 mmol) and water (0.5 g) and stirred at 25 °C for 22 h. The reaction mixture was diluted with dichloromethane, filtered, and the solid washed with dichloromethane (2 × 25 cm^3). The organic layer was dried (MgSO$_4$) and concentrated to yield the product.

Acidic hydrolysis of the reaction mixture yielded products which were free of the 2-oxoalkylphosphonate even when this reagent was present in excess.

Yields were determined by g.l.c. (error ± 2%) except for the reaction of (1) and (3b) with the system NaH–DME due to the similar retention times of (3b) and (4b) (Table 1, entry 4). In this case the conversion was deduced by ^{1}H n.m.r. spectroscopy (Tables 1 and 2). The following conditions were used: (a) column temperature 130 °C, gas flow (N$_2$) 50 cm^3 min^{-1} for (4a), (4b), (4d), and (4e), retention times: (1), 5.2 min; (2) 9.7 min; (3a), 23.4 min; (3b), 33.2 min; (4a), 35.4 min; (4b), 34.3 min; (4d), 59.4 min; (4e), 53.7 min; (b) column temperature 185 °C, gas flow (N$_2$) 55 cm^3 min^{-1}, for (4c) and (4f), retention times: (1), 1.2 min; (2), 1.8 min; (3c), 39.9 min; (4c), 43.5 min; (4f), 69.5 min.

Estimation of the mixture of (4b), (Z)-(5) and (E)-(5) obtained using NaH–DME at 40 °C (Scheme 2) was carried out by g.l.c. using the following conditions: initial temperature 110 °C (15 min), end temperature 175 °C, heating rate 30 °C min^{-1}, retention times: (Z)-(5), 22.6 min; (E)-(5), 33.8 min; (4b), 26.2 min.

Purification and Characterization of α-Enones.—α-Enones (4a–f) were purified by silica gel chromatography [30:1 (w/v) adsorbent product ratio] using light petroleum–ether (97:3) as eluant. α-Enones (4e, f) are solids and the remaining α-enones were obtained as liquids. Their purity was tested by g.l.c., ^{1}H n.m.r. spectroscopy, and analytical data [for solids (4e) and (4f)].

Characterization was carried out by mass spectrometry, i.r., and ^{1}H and ^{13}C n.m.r. spectroscopy. The molecular ion of α-enones (4d–f) was not observed in mass spectra and this behaviour was attributed to a very favourable McLafferty rearrangement with loss of isobutene (M^+ − 56) due to the presence of the Bu^t group in the γ-position. The ^{1}H and ^{13}C n.m.r. magnetic parameters are collected in Tables 1 and 2.

(E)-(5RS)-5-Phenylhex-3-en-2-one (4a). $\nu_{max.}$(CHCl$_3$) 1 675(CO) and 1 620 cm^{-1}(C=C); m/z 174(M^+, 21%), 159 (14), 131 (100), 115 (21), 91 (41), 77 (15), 51 (15), and 43 (97).

(E)-(6RS)-2,2-Dimethyl-6-phenylhept-4-en-3-one (4b). $\nu_{max.}$(CHCl$_3$) 1 690 (CO) and 1 620 cm^{-1} (C=C); m/z 216 (M^+, 7%), 159 (100), 144 (26), 141 (25), 131 (40), 115 (20), 111 (17), 91 (27), 77 (11), 57 (34), 43 (23), and 41 (38).

(E)-(4RS)-1,4-Diphenylpent-2-en-1-one (4c). $\nu_{max.}$(CHCl$_3$) 1 675–1 660 (CO) and 1 620–1 600 cm^{-1} (C=C); m/z 236 (M^+, 12%), 131 (26), 115 (14), 105 (100), 91 (11), 77 (42), and 51 (17).

(E)-(5RS)-6,6-Dimethyl-5-phenylhept-3-en-2-one (4d). $\nu_{max.}$(CHCl$_3$) 1 675 (CO) and 1 620 cm^{-1} (C=C); m/z 160 (M^+ −56, 100%) 145 (24), 117 (52), 115 (25), 91 (11), 57 (45), 43 (96), and 41 (40).

(E)-(6RS)-2,2,7,7-Tetramethyl-6-phenyloct-4-en-3-one (4e). M.p. 82–84 °C (from MeOH) (Found: C, 83.55; H, 10.2.

$C_{18}H_{26}O$ requires C, 83.7; H, 10.1%); $v_{max.}$(CHCl$_3$) 1 685 (CO) and 1 620 cm^{-1} (C=C); m/z 202 (M^+ − 56, 99%), 145 (85), 117 (43), 115 (28), 91 (12), 57 (100), and 41 (66).

(*E*)-(4*RS*)-5,5-Dimethyl-1,4-diphenylhex-2-en-1-one (**4f**). M.p. 99–101 °C (from MeOH) (Found: C, 86.4; H, 7.75. $C_{20}H_{22}O$ requires C, 86.3; H, 7.9%); $v_{max.}$(CHCl$_3$) 1 665 (CO) and 1 615–1 600 cm^{-1}(C=C); m/z 222 (M^+ − 56, 100%), 221 (34), 115 (25), 105 (56), 91 (8), 77 (37), 57 (26), and 41 (25).

The (*E*)- and (*Z*)-isomers of 2,2-dimethyl-6-phenylhept-5-en-3-one (**5**) were characterized by their ^{1}H n.m.r. spectra: (*E*) δ 1.18 (9 H, s, Bu^t), 2.02 (3 H, br s, Me), 3.40 (2 H, d, *J* 6.8 Hz, 4-H), 5.94 (1 H, m, *J* 6.8 and 1.1 Hz, 5-H), and 7.26 (5 H, m, Ph); (*Z*) δ 1.02 (9 H, s, Bu^t), 2.02 (3 H, br s, Me), 3.15 (2 H, d, *J* 7.2 Hz, 4-H), 5.60 (1 H, m, *J* 7.2 and 1.1 Hz), and 7.26 (5 H, m, Ph).

^{31}P *Spectroscopic Measurements.*—Solutions of the anionic species produced from 2-oxoalkylphosphonates (**3**) by the action of barium hydroxide C-200 in 1,4-dioxane were prepared under the following reaction conditions. Barium hydroxide C-200 (0.25 mmol), 2-oxoalkylphosphonate (**3**) (0.5 mmol), and 1,4-dioxane (2 cm^3 with 1% of water) were stirred at 70 °C for 10 min and the mixture was filtered through a 0.5 μm millipore FH filter. ^{31}P N.m.r. spectra of 2-oxoalkylphosphonates (**3**) were also registered in the same solvent. All the spectra were recorded at 303 K: δ (**3a**) 19.8, (**3b**) 21.1, and (**3c**) 19.9 p.p.m.; anionic species from (**3a**) 30.1, (**3b**) 35.4, and (**3c**) 32.9 p.p.m.

References

1 J. I. C. Cadogan, ed., 'Organophosphorus Reagents in Organic Synthesis,' Academic Press, New York, 1979.
2 (*a*) H. J. Bestmann, *Pure Appl. Chem.*, 1980, **52**, 771; (*b*) Y. Le Bigot, M. Delmas, and A. Gaset, *Inform. Chim.*, 1984, **251**, 123.
3 (*a*) J. Boutagy and R. Thomas, *Chem. Rev.*, 1974, **74**, 87; (*b*) W. S. Wadsworth, *Org. Reactions*, 1978, **25**, 73; (*c*) K. B. Becker, *Synthesis*, 1983, 341.
4 (*a*) W. E. McEwen, B. D. Beaver, and J. V. Cooney, *Phosphorus Sulfur*, 1985, **25**, 255; (*b*) B. E. Maryanoff, A. B. Reitz, M. S. Mutter, R. R. Inners, H. R. Almond, Jr., R. R. Whittle, and R. A. Olofson, *J. Am. Chem. Soc.*, 1986, **108**, 7664; (*c*) Y. Le Bigot, M. Delmas, and A. Gaset, *Tetrahedron*, 1986, **42**, 339; (*d*) Y. Le Bigot, R. El Gharbi, M. Delmas, and A. Gaset, *ibid.*, p. 3813; (*e*) Y. Le Bigot, M. Delmas, and A. Gaset, *ibid.*, 1988, **44**, 1057.
5 (*a*) G. Etemad-Moghadam and J. Seyden-Penne, *Tetrahedron*, 1984, **40**, 5153; (*b*) M. W. Rathke and M. Nowak, *J. Org. Chem.*, 1985, **50**, 2624.
6 (*a*) C. Piechucki, *Synthesis*, 1974, 869; (*b*) C. Piechucki, *ibid.*, 1976, 187; (*c*) E. D'Incan and J. Seyden-Penne, *ibid.*, 1975, 516.
7 (*a*) J. Villieras and M. Rambaud, *Synthesis*, 1983, 300; (*b*) J. Villieras and M. Rambaud, *ibid.*, 1984, 406.
8 F. Texier-Boullet and A. Foucaud, *Synthesis*, 1979, 884.
9 J. Villieras, M. Rambaud, and B. Kirshleger, *Phosphorus Sulfur*, 1983, **14**, 385.
10 Z. Mouloungui, M. Delmas, and A. Gaset, *Synth. Commun.*, 1984, **14**, 701.
11 F. Texier-Boullet, D. Villemin, M. Ricard, H. Moison, and A. Foucaud, *Tetrahedron*, 1985, **41**, 1259.
12 (*a*) J. V. Sinisterra, Z. Mouloungui, M. Delmas, and A. Gaset, *Synthesis*, 1985, 1097; (*b*) J. V. Sinisterra, M. E. Barredon, Z. Mouloungui, M. Delmas, and A. Gaset, *React. Kinet. Catal. Lett.*, 1985, **29**, 41; (*c*) J. V. Sinisterra, A. Alcántara, and J. M. Marinas, *J. Colloid Interface Sci.*, 1987, **115**, 520; (*d*) J. V. Sinisterra, A. Fuentes, and J. M. Marinas, *J. Org. Chem.*, 1987, **52**, 3875.
13 H. Moison, F. Texier-Boullet, and A. Foucaud, *Tetrahedron*, 1987, **43**, 537.
14 J. V. Sinisterra, F. Garcia-Blanco, M. Iglesias, and J. M. Marinas, *React. Kinet. Catal. Lett.*, 1984, **25**, 277.
15 J. Barrios, J. M. Marinas, and J. V. Sinisterra, *Bull. Soc. Chim. Belg.*, 1986, **95**, 107.
16 M. Iglesias, J. M. Marinas, and J. V. Sinisterra, *Tetrahedron*, 1987, **43**, 2335.
17 J. V. Sinisterra, A. Garcia-Raso, J. A. Cabello, and J. M. Marinas, *Synthesis*, 1984, 502.
18 C. Alvarez Ibarra, M. S. Arias, G. Bañón, M. J. Fernández, M. Rodriguez, and J. V. Sinisterra, *J. Chem. Soc., Chem. Commun.*, 1987, 1509.
19 (*a*) C. H. Heathcock, S. Kiyooka, and T. A. Blumenkopf, *J. Org. Chem.*, 1984, **49**, 4214; (*b*) C. H. Heathcock and D. E. Uehling, *ibid.*, 1986, **51**, 279.
20 G. Sturtz, *Bull. Soc. Chim. Fr.*, (*a*) 1964, 2349; (*b*) 1967, 2477.
21 J. Sasaki, *Bull. Chem. Soc. Jpn.*, 1967, **40**, 2967.
22 J. Pine and M. J. Skoglund, *J. Org. Chem.*, 1982, **47**, 4758.
23 J. V. Sinisterra, M. D. Jimenez, M. Iglesias, and J. M. Marinas, *React. Kinet. Catal. Lett.*, 1987, in the press.
24 A. Sosunova, A. P. Kilimov, and V. Smirnov, *Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.*, 1970, **13**, 734 (*Chem. Abstr.*, 1970, **73**, 65842c).
25 G. Agnes, and J. Songstad, *Acta Chem. Scand.*, 1964, **18**, 655.
26 T. Strzalko, J. Seyden-Penne, F. Froment, J. Corset, and M. P. Simonnin, *J. Chem. Soc., Perkin Trans. 2*, 1987, 783.
27 L. M. Weinstock, J. M. Stevenson, S. A. Tomellini, S. H. Pan, T. Utne, R. B. Jobson, and D. F. Reinhold, *Tetrahedron Lett.*, 1986, **27**, 3845.
28 (*a*) T. Mukaiyama, K. Saigo, and T. Izawa, *Japan Kokai*, 76, **41**, 315 (CL C07C47/17) 07 Apr., 1976; (*Chem. Abstr.*, 1976, **85**, 123591f); (*b*) T. Yoshida and J. B. Hall, *USP*, 4, 169, 109 (CL 260-586C; C07C45/00) 25 Sept., 1979, (*Chem. Abstr.*, 1980, **92**, 6069a).
29 (*a*) N. S. Bhacca and D. H. Williams, 'Applications of NMR Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964; (*b*) L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd edn. Pergamon Press, London, 1978.
30 K. B. Wiberg and S. L. Schreiber, *J. Org. Chem.*, 1988, **53**, 783.
31 R. M. Lequan, M. J. Pouet, and M. P. Simonnin, *Org. Magn. Reson.*, 1975, **7**, 392.
32 A. Garcia-Raso, J. A. Garcia-Raso, B. Campaner, R. Mestres, and J. V. Sinisterra, *Synthesis*, 1982, 1037.
33 F. Mathey and Ph. Savignac, *Tetrahedron*, 1978, **34**, 649.
34 E. P. Lodge and C. H. Heathcock, *J. Am. Chem. Soc.*, 1987, **109**, 3353.
35 C. Alvarez Ibarra, R. Perez-Ossorio, M. L. Quiroga, M. S. Arias Perez, M. J. Fernández, and E. Moya, *An. Quim.*, 1983, **79C**, 350.
36 (*a*) D. J. Reif and H. O. House, *Org. Synth. Coll.*, 1963, vol. 4, p. 375; (*b*) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, 1965, **87**, 1353.