Reactions of Anions from α-Diphenylphosphinoyl Ketones with Electrophiles

Richard S. Torr and Stuart Warren *
University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW

Anions from α-$Ph_2P(O)$-ketones do not give Horner–Wittig reactions but do react with alkyl halides, including α-halogenocarbonyl compounds, and Michael acceptors. The products may be stereoselectively reduced.

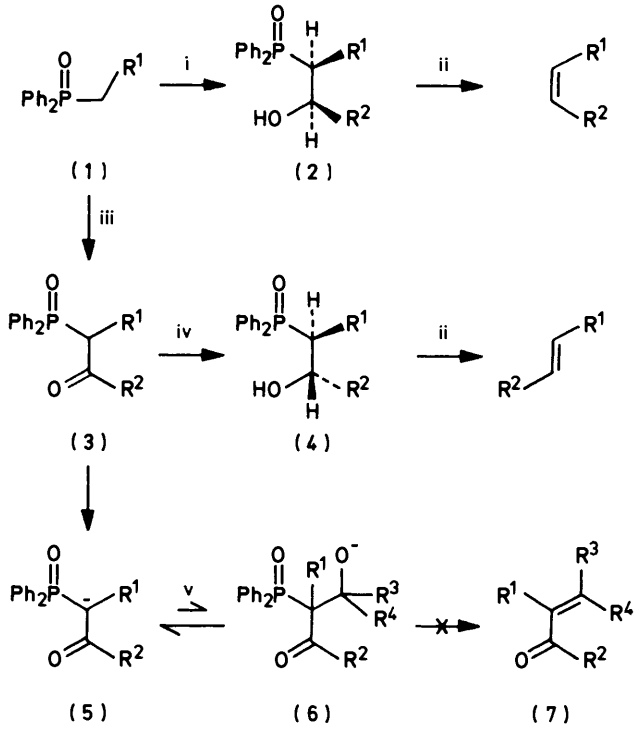
Anions of alkyl(diphenyl)phosphine oxides (1) react [1] with aldehydes to give predominantly *erythro*-alcohols (2) which eliminate $Ph_2PO_2^-$ in base to give (*Z*)-alkenes (Scheme 1). Acylation of the anions of (1) with esters [2] gives α-diphenylphosphinoyl ketones (3) and hence [1] (*E*)-alkenes *via* *threo*-alcohols (4). The more stable anions (5) of ketones (3) do not react with aldehydes or ketones to give enones (7). This is presumably because the 'aldol' anions (6) are unstable and revert to (5), since we now report that anions (5) react satisfactorily with other electrophiles, *e.g.* alkyl halides, in reactions where the products cannot easily revert to starting materials.

Reactions with Aldehydes and Ketones.—The anion from ketone (3; $R^1 = H$, $R^2 = Me$) could be formed with $NaNH_2$, NaOMe, LDA (lithium di-isopropylamide), NaH, BuLi, KOH, or Bu^{t}OK in THF (tetrahydrofuran), DMF (dimethylformamide), or methanol, but failed to react with benzaldehyde, *p*-methoxybenzaldehyde, acetaldehyde, or cyclohexanone at 0 °C, room temperature, or under reflux. Reactions did occur with *p*-nitrobenzaldehyde but only to give tars from which no products were isolated. Reactions under phase-transfer conditions (CH_2Cl_2, water, NaOH, tetra-alkylammonium salts) also failed. Some reactions gave diphenylphosphonic acid but this was formed by decomposition of ketone (3), not as a result of the Horner–Wittig reaction, as the electrophile was unaffected.

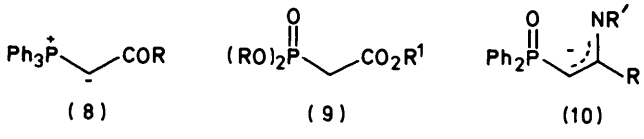
The less reactive ylides (8) are also reluctant to take part in olefination reactions [3] but the phosphonates (9) are commonly used to make unsaturated esters.[4] Anions of (9) must be about as reactive as the anions (5) but the unfavourable equilibrium is driven over by the elimination of phosphate in this one-step method. The balance between anion reactivity and formation of a new P–O bond must be close in all cases and unfavourable for the phosphine oxides.

Ketones (3) can be used to make the enones (7) after conversion into the corresponding enamines. Aguiar [5] has shown that anions (10) of these enamines combine satisfactorily with aldehydes and ketones in Horner–Wittig reactions.

Reactions with Alkyl Halides.—Anions formed from ketones (11) with NaH, MeONa–MeOH, Bu^{t}OK, LDA, LiH, or BuLi gave alkylation products (Table 1). The lithium bases needed TMEDA (tetramethylethylenediamine) for best results (*e.g.* entry 3, Table 1), and the preferred conditions are NaH in THF at room temperature. Methyl iodide, benzyl and prenyl (3-methylbut-2-enyl) bromides, and α-halogenocarbonyl compounds gave good yields of products, though there was much dialkylation with prenyl bromide (entry 4). There was no reaction with n-butyl bromide, even with iodide ion catalysis or in DMF solution, nor with ethyl 2-bromobutanoate.



Scheme 1. *Reagents:* i, BuLi, then R^2CHO; ii, NaH, DMF; iii, BuLi, then R^2CO_2Et; iv, $NaBH_4$; v, R^3COR^4



Alkylation of ketones (11) (Scheme 2) is, then, an alternative route to acylation of (1) in the synthesis of ketones (3) and hence (*E*)-alkenes. For example, the product of entry 7, Table 1 (3; $R^1 = Me$, $R^2 = Ph$) gives 89% *threo*-(4) on reduction with $NaBH_4$ and elimination with NaH in DMF then gives all-(*E*)-PhCH=CHMe in 81% yield.[1]

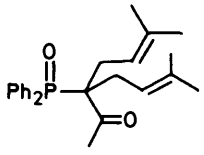
A second alkylation can be carried out on the products of the first alkylation (Table 2) but the yields are good only with α-halogenocarbonyl compounds and even with these electrophiles *O*-alkylation is a problem. The aromatic ketone (3; $R^1 = Me$, $R^2 = Ph$) gives mostly the enol ether (13) with ethyl bromoacetate (entry 4, Table 2).

Hydroxy ketones, *e.g.* (14), are available [1,2] by acylation of

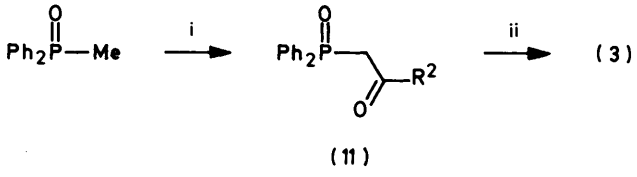
Table 1. Alkylation of α-diphenylphosphinoyl ketones (11)

Entry	R^2	R^1X	Conditions [a]	Yield (%) of (3)
1	Me	MeI	A	72
2	Me	MeI	B	78
3	Me	MeI	C	67
4	Me	$Me_2C{=}CHCH_2Br$	A	28 [b]
5	Me	$PhCOCH_2Br$	A	74
6	Me	$BrCH_2CO_2Et$	A	79
7	Ph	MeI	B	65
8	Ph	$PhCH_2Br$	B	60
9	Ph	$BrCH_2CO_2Et$	A	70 [c]
10	Ph	ICH_2CO_2Et	D	66 [c]

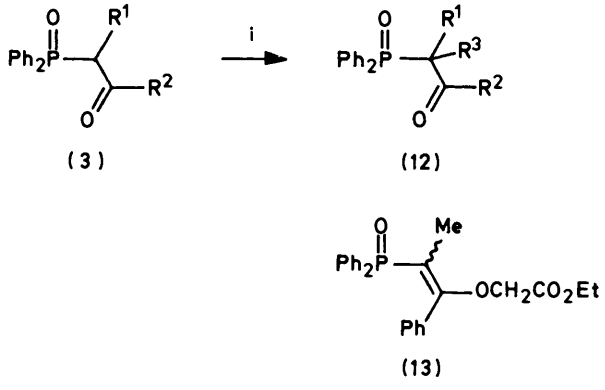
[a] A: NaH, THF, room temperature, B: MeONa, THF, room temperature, C: BuLi, TMEDA, THF, under reflux, D: LiH, THF, room temperature. [b] Plus 47% diadduct:



[c] Plus a trace (<5%) of *O*-alkylated product.



Scheme 2. *Reagents:* i, BuLi, then R^2CO_2Et; ii, base, then R^1X



Reagents: i, base, then R^3X

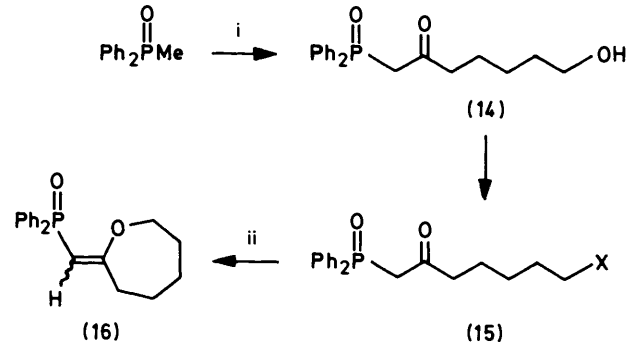
phosphine oxides with lactones (Scheme 3), and we attempted the intramolecular alkylation of ketone (14). The corresponding bromide (15; X = Br) and tosylate (15; X = $OSO_2C_6H_4Me$-*p*) were easily prepared but gave only *ca.* 35% of a 1 : 1 mixture of geometrical isomers of the enol ether (16). Evidently the enolate anion of (15) prefers to act in a 7-*exo* rather than a 7-*endo*-trig manner.[6]

Michael Additions.—The unsubstituted ketone (11; R^2 = Me) gives a moderate yield (47%) of the Michael adduct (17) with methyl acrylate, but ketone (3; $R^1 = R^2$ = Me) gives only the cyclohexanedione (18). The initial product of Michael

Table 2. Alkylation of substituted ketones (3)

Entry	R^2	R^1	R^3X	Conditions [a]	Yield (%) of (12)
1	Me	Me	MeI	B	43
2	Me	Me	$BrCH_2CO_2Et$	A	80
3	Me	Me	ICH_2CO_2Et	D	30
4	Ph	Me	$BrCH_2CO_2Et$	A	25 [b]

[a] See Table 1. [b] And 54% of *O*-alkylated product (13).



Scheme 3. *Reagents:* i, BuLi, then $\overline{O{\cdot}[CH_2]_5{\cdot}CO}$; ii, base

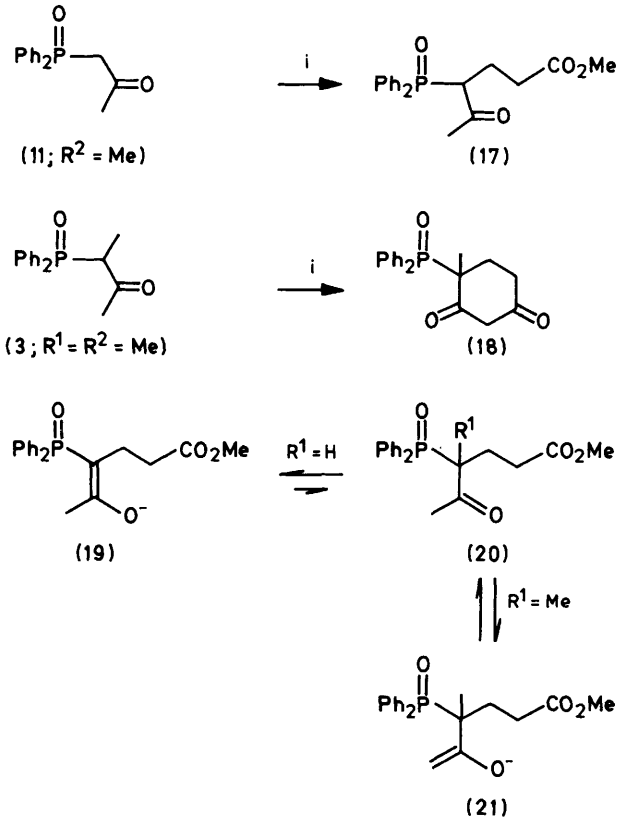
addition (20), can form a stable enolate (19) if R^1 = H but if R^1 = Me equilibration to (21), cyclisation to (18), and formation of its stable enolate occurs instead. Michael additions failed between (11; R^2 = Me) and pent-3-en-2-one and between (3; R^1 = Me, R^2 = Ph) and methyl acrylate.

Dianions.—Treatment of ketone (11; R^2 = Me) with NaH in THF followed by BuLi generates dianion (22) which reacts at the carbon atom γ to phosphorus with alkyl halides (Scheme 4). Moderate yields of products are accompanied by recovered starting material.

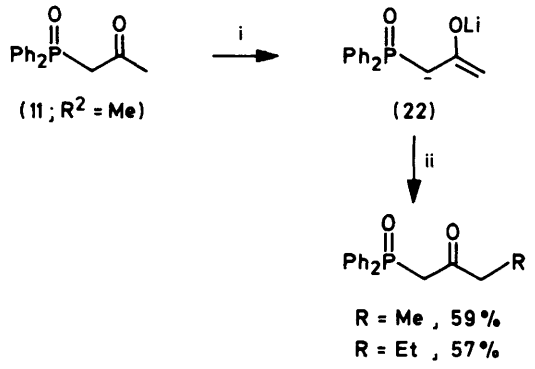
β-*Diphenylphosphinoyl* γ-*Lactones.*—The products (23) of alkylation with bromoacetate esters (entries 6, Table 1 and 2, Table 2) are chemo- and stereo-selectively reduced by sodium borohydride in methanol at room temperature to give lactones (24) in high yield.

When R = H, one diastereoisomer of lactone (24) predominates by 3 : 1. We have already reported [7] a similar reaction on α-(phenylthio) ketones (25) where the *cis*-lactone (26) was always favoured, sometimes completely. We conclude that the same stereoselectivity, *i.e.* in favour of lactone (24A) over (24B), is observed here for the following reasons.

(a) Borohydride reduction of ketones (3) is *threo*-selective and lactone (24A) is the '*threo*' isomer, *i.e.* that isomer which would give an (*E*)-alkene on completion of the Horner–Wittig reaction. (b) The ^1H n.m.r. spectrum of lactone (24; R = Me) can be resolved sufficiently for the coupling constants (Table 3) to be measured. The conformational drawings (27A) and (27B) put the large Ph_2PO group in a pseudo equatorial position and agree both with models and with an *X*-ray crystal structure [7] of lactone (26; R = Bu^t). The models predict P–C–C–H^C torsion angles of 70—80° for (24A) and 30—40° for (24B). Benezra's equations [8] for the variation of $^3J_{PH}$ with dihedral angle give *J* 0—2 Hz for an angle of 70—80° and 10—14 Hz for one of 30—40°. The observed values fit these predictions well and are sup-



Reagents: i, NaH, then CH_2=$CHCO_2Me$

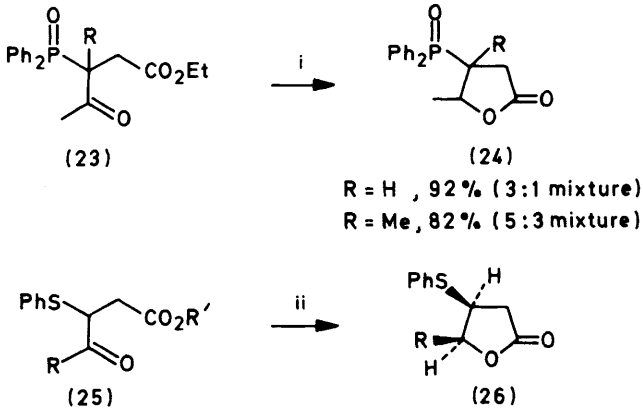


Scheme 4. *Reagents:* i, NaH, THF; then BuLi; ii, RI, then NH_4Cl

ported by the values observed for $^3J(PH^A)$ and $^3J(PH^B)$. (c) Heating the 5 : 3 mixture of lactones (24A) and (24B) (R = Me) in 1 : 1 n-butanol–toluene containing toluene-*p*-sulphonic acid under reflux for two weeks led to recovered lactone (24) in which the isomeric ratio had changed to 1 : 2 in favour of (24B), the isomer having Ph_2PO and Me^C *trans*. We assume that this occurs *via* cation (28).

The reduction of keto esters (23) therefore provides a link between the reduction of ketones (3) in our (*E*)-selective olefin synthesis [1] and the reduction of keto esters (25) in our butenolide synthesis.[7] We believe all three results are best explained by a stereoselective approach of borohydride to the less hindered face of the ketone in Felkin's model (29) for the transition state.[9]

Rearrangement of Lactones.—Lactones (30; Z = PhS)



Reagents: i, $NaBH_4$, MeOH; ii, $NaBH_4$

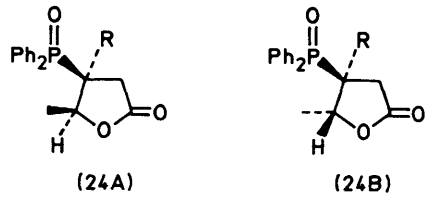
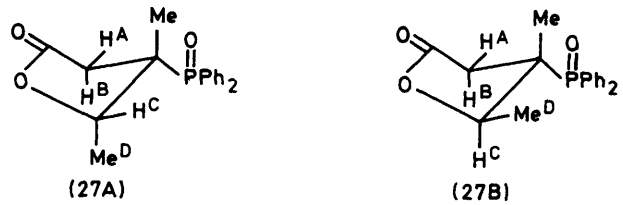
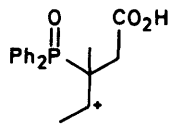


Table 3. ^1H N.m.r. coupling constants (Hz) for lactones (24A) and (24B)

	$^3J(PH^A)$	$^3J(PH^B)$	$^3J(PH^C)$	$^3J(H^CH^D)$
(24A)	2.5	11	2.5	7
(24B)	2.5	13	9	7

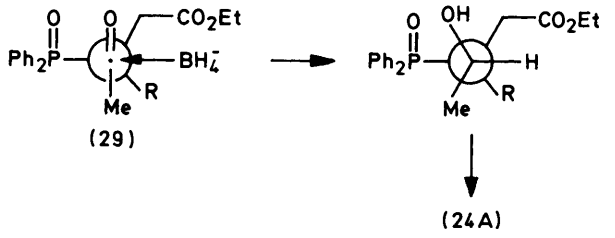


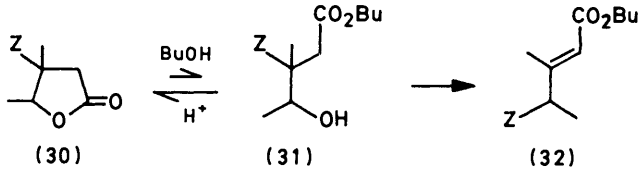


and we had hoped to synthesise the corresponding phosphine oxides (32; Z = Ph_2PO) by rearrangement of the lactone (30; Z = Ph_2PO). However, even after three weeks under reflux in chlorobenzene containing butanol and toluene-*p*-sulphonic acid, only 4% of the ester (32; Z = Ph_2PO) could be isolated and most of the starting material had been destroyed. Under milder conditions no rearrangement occurred. The equilibrium between (30; Z = Ph_2PO) and (31; Z = Ph_2PO) is evidently too unfavourable for the more reluctant Ph_2PO group to migrate.

Experimental

M.p.s were determined on a Reichart Kofler hot stage and





Associated HA100D, EM360A, Hitachi Perkin-Elmer R24A, and CFT20 machines. I.r. spectra were recorded on Perkin-Elmer 257 and 297 machines as thin films, Nujol mulls, or *chloroform solution* spectra. Mass spectra were run on an A.E.I. MS30 instrument, using a DS 50S data system for high-resolution scans.

Thin-layer chromatography (t.l.c.) was run on silica gel GF_{254} (0.25 mm) plates, preparative thick-layer chromatography (p.l.c.) on silica gel GF_{254} (1 mm) plates, and column chromatography on Merck silica Kieselgel 60 with EtOAc as eluant; compounds were visualised by u.v. light except where otherwise stated. Materials were extracted from thick-layer plates with EtOAc. Solvents for chromatography were distilled before use.

3-(*Diphenylphosphinoyl*)*butan-2-one* (3; $R^1 = R^2 = Me$) (*Method B*).—The ketone[2] (11; $R^2 = Me$) (500 mg, 1.94 mmol) was stirred with sodium methoxide (120 mg, 2.2 mmol) in dry THF (5 ml) at room temperature under nitrogen for 5 min, then methyl iodide (0.32 g, 2.2 mmol) was added. The mixture was stirred at this temperature for 2 h and was then poured into aqueous NH_4Cl (20 ml). The layers were separated, the aqueous layer was extracted with EtOAc (2 × 20 ml), and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a pale-yellow oil. P.l.c. on silica (development with EtOAc) gave the ketone (3; $R^1 = R^2 = Me$) (410 mg, 78%), m.p. 132—134 °C (lit.,[2] 117—119 °C) (Found: C, 70.7; H, 6.3; P, 11.4. $C_{16}H_{17}O_2P$ requires C, 70.6; H, 6.25; P, 11.4%). I.r., n.m.r., and mass spectra were identical with those previously reported.[2]

Reaction of Diphenylphosphinoylpropan-2-one with Prenyl Bromide.—The ketone (11; $R^2 = Me$) (258 mg, 1 mmol) was stirred with sodium hydride (60 mg, 1.25 mmol) in dry THF under nitrogen at 0 °C for 15 min. At this temperature, 1-bromo-3-methylbut-2-ene (prenyl bromide) (0.17 g, 1.14 mmol) was added dropwise and the solution was stirred overnight at room temperature. Aqueous NH_4Cl (10 ml) was then added, the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 ml). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a yellow oil. P.l.c. on silica (development with EtOAc) gave 3-*diphenylphosphinoyl*-6-*methylhept*-5-*en*-2-*one* (3; $R^1 = Me_2C{=}CHCH_2$, $R^2 = Me$) (92 mg, 28%) as needles, m.p. 134—136 °C (from EtOAc); R_F 0.38 (EtOAc); δ_H ($CDCl_3$) 1.54 (3 H, s, Me), 1.62 (3 H, s, Me), 2.18 (3 H, s, COMe), 2.30—3.10 (2 H, m, $PCHC\mathit{H}_2$), 3.62 (1 H, ddd, J_H 4, J_H 8, and J_{PH} 12 Hz, $PC\mathit{H}CH_2$), 4.98 (1 H, br t, J_{HH} *ca.* 7 Hz, =CH), and 7.40—7.98 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 700 (C=O), 1 440 (P–Ph), and 1 180 cm^{-1} (P=O); *m/z* 326 (M^+, 10%), 243 [$Ph_2P(O)CH_2CO^+$, 44], 202 [$Ph_2P(O)H^+$, 100], and 201 (Ph_2PO^+, 73) (Found: C, 73.1; H, 6.9. $C_{20}H_{23}O_2P$ requires C, 73.6; H, 7.1%) and 3-diphenylphosphinoyl-6-methyl-3-(3-methylbut-2-enyl)hept-5-en-2-one (12; $R^1 = R^3 = Me_2C{=}CHCH_2$, $R_2 = Me$) (184 mg, 47%) as an oil, R_F 0.52 (EtOAc); δ_H ($CDCl_3$) 1.52 (6 H, s, $Me_2C{=}$), 1.58 (6 H, s, $Me_2C{=}$), 2.05 (3 H, s, MeCO), 2.58—3.16 (4 H, m, 2 × CH_2), 4.92 (2 H, br t, J_{HH} *ca.* 8 Hz, 2 × =CH), and 7.32—8.04 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 700 (C=O), 1 440 (P–Ph), and 1 185 cm^{-1} (P=O); *m/z* 394 (M^+, 6%) 202 [$Ph_2P(O)H^+$, 100], and 201 (Ph_2PO^+, 87).

3-*Diphenylphosphinoyl*-1-*phenylpentane*-1,4-*dione* (3; $R^1 = PhCOCH_2$, $R^2 = Me$) (*Method A*).—1-(Diphenylphosphinoyl)propan-2-one (11; $R^2 = Me$) (258 mg, 1 mmol) was stirred in dry THF (10 ml) at 0 °C under nitrogen with sodium hydride (55 mg, 1.15 mmol) for 0.25 h. A solution of phenacyl bromide (0.22 g, 1.1 mmol) in dry THF (2 ml) was then added, and the mixture was stirred for 0.5 h at room temperature, during which time a white precipitate formed. The mixture was poured into aqueous NH_4Cl (20 ml), separated, and the aqueous layer was extracted with EtOAc (3 × 15 ml), the combined organic extracts dried (Na_2SO_4) and evaporated under reduced pressure to give a pale-yellow solid. P.l.c. on silica (development with EtOAc) gave the *diketone* (282 mg, 74%), m.p. 155—157 °C (from EtOAc) (Found: C, 73.1; H, 5.7. $C_{23}H_{21}O_3P$ requires C, 73.4; H, 5.6%); R_F 0.50 (EtOAc); δ_H ($CDCl_3$) 2.10 (3 H, s, Me), 3.26 (1 H, ddd, J_{AB} 18, J_{AC} 2, and J_{PA} 8 Hz, $PCH_CC\mathit{H}_AH_B$), 4.00 (1 H, ddd, J_{AB} 18, J_{BC} 11, and J_{PB} 4 Hz, $PHC_CCH_A\mathit{H}_B$), 4.48 (1 H, ddd, J_{AB} 2, J_{BC} 11, and J_{PC} 15 Hz, $PC\mathit{H}_CCH_AH_B$), and 7.30—8.04 (total 15 H, m, Ph, and Ph_2PO); $\nu_{max.}$ 1 710 (C=O), 1 690 (PhC=O), 1 440 (P–Ph), and 1 190 cm^{-1} (P=O); *m/z* 376 (M^+, 0.3%), 333 [(M – MeCO)$^+$, 9], 271 [(M – PhCO)$^+$, 12], 229 [$Ph_2P(O)CH_2CH_2^+$, 59], and 201 (Ph_2PO^+, 100) (Found: M^+, 376.1217. $C_{23}H_{21}O_3P$ requires M, 376.1218).

Ethyl 3-*Diphenylphosphinoyl*-4-*oxopentanoate* (23; R = H).—1-(Diphenylphosphinoyl)propan-2-one (11; $R^2 = Me$) (516 mg, 2 mmol) was stirred in dry THF (10 ml) at 0 °C under nitrogen with sodium hydride (110 mg, 2.3 mmol) for 0.5 h, ethyl bromoacetate (0.37 g, 2.2 mmol) was then added dropwise, the mixture was stirred for 2 h at 0 °C and was then warmed to room temperature. Distilled water (20 ml) was added, the layers were separated, the aqueous layer was extracted with EtOAc (3 × 20 ml), and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a white solid which, on recrystallisation from EtOAc, gave the *keto ester* (23; R = H) (543 mg, 79%), m.p. 116—118 °C (Found: C, 66.3; H, 6.0. $C_{19}H_{21}O_4P$ requires C, 66.3; H, 5.8%); R_F 0.33 (EtOAc); δ_H ($CDCl_3$) 1.17 (3 H, t, J_{HH} 7 Hz, $CH_2\mathit{Me}$), 2.54 (1 H, ddd, J_{AB} 18, J_{AC} 3, and J_{PA} 9 Hz, $PCH_CC\mathit{H}_AH_B$), 3.18 (1 H, ddd, J_{AB} 18, J_{BC} 12, and J_{PB} 6 Hz, $PCH_CCH_A\mathit{H}_B$), 4.05 (2 H, q, J_{HH} 7 Hz, $C\mathit{H}_2Me$), 4.22 (1 H, ddd, J_{AC} 3, J_{BC} 12, and J_{PC} 17 Hz, $PC\mathit{H}_CCH_AH_B$), and 7.36—8.00 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 740 (CO_2Et), 1 710 (C=O), 1 440 (P–Ph), and 1 185 cm^{-1} (P=O); *m/z* 344 (M^+, 9%), 298 [(M – EtOH)$^+$, 40], 271 [(M – CO_2Et)$^+$, 44], and 201 (Ph_2PO^+, 100).

2-*Diphenylphosphinoyl*-1-*phenylpropan*-1-*one* (3; $R^1 = Me$, $R^2 = Ph$) (*Method B*).—The ketone[2] (11; $R^2 = Ph$) (160 mg, 0.5 mmol) was stirred with sodium methoxide (30 mg, 0.55 mmol) in dry THF (5 ml) at room temperature under nitrogen for 5 min, then methyl iodide (0.08 g, 0.55 mmol) was added. The mixture was stirred at room temperature for 3 h and was

then poured into aqueous NH_4Cl (20 ml). The layers were separated, the aqueous layer was extracted with EtOAc (2 × 20 ml), and the combined organic aqueous extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give an oil. P.l.c. on silica (development with EtOAc) gave the ketone (109 mg, 65%), m.p. 152—154 °C (from EtOAc–4% methanol) (lit.,[11] 154—155 °C); i.r.,[11] n.m.r.,[11] and mass spectra [2] agree with those previously reported.

1,3-*Diphenyl*-2-(*diphenylphosphinoyl*)*propan*-1-*one* (3; R^1 = $PhCH_2$, R^2 = Ph) (*Method B*). The ketone (11; R^2 = Ph) (160 mg, 0.5 mmol) was stirred with sodium methoxide (30 mg, 0.55 mmol) in dry THF (5 ml) at room temperature under nitrogen for 5 min, then benzyl bromide (85 mg, 0.55 mmol) and a catalytic amount of crushed potassium iodide (10 mg) were added. The mixture was heated under reflux for 2 d, cooled, and poured into aqueous NH_4Cl (20 ml). The layers were separated, the aqueous layer was extracted with EtOAc (2 × 20 ml), and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a yellow oil. P.l.c. on silica (EtOAc) gave the ketone (124 mg, 60%), m.p. 202—204 °C (lit.,[2] 202—204 °C); spectra were identical with those previously published [2] (Found: C, 79.1; H, 5.7. $C_{27}H_{23}O_2P$ requires C, 79.0; H, 5.65%).

Ethyl 3-*Diphenylphosphinoyl*-4-*oxo*-4-*phenylbutanoate* (3; R^1 = CH_2CO_2Et, R^2 = Ph) (*Method A*).—The ketone (11; R^2 = Ph) (320 mg, 1 mmol) was stirred in dry THF (10 ml) with sodium hydride (53 mg, 1.1 mmol) for 0.5 h at 0 °C under nitrogen. Ethyl bromoacetate (0.18 g, 1.1 mmol) was added dropwise over a period of 1 min, and the mixture was then stirred for 6 h at room temperature, poured into water (50 ml), the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 15 ml). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a white solid. P.l.c. on silica (EtOAc) gave the *keto ester* (284 mg, 70%), m.p. 130—132 °C (from EtOAc) (Found: C, 71.0; H, 5.85; P, 7.7. $C_{24}H_{23}O_4P$ requires C, 70.9; H, 5.7; P, 7.6%); R_F 0.39 (EtOAc); δ_H ($CDCl_3$) 1.13 (3 H, t, J_{HH} 7 Hz, CH_2Me), 2.90 (1 H, ddd, J_{AB} 18, J_{HA} 3, and J_{PA} 9 Hz, $PCHCH_AH_B$), 3.44 (1 H, ddd, J_{AB} 18, J_{HB} 11, and J_{PB} 5 Hz, $PCHCH_AH_B$), 4.03 (2 H, q, J_{HH} 7 Hz, CH_2Me), 5.09 (1 H, ddd, J_{HA} 3, J_{HB} 11, and J_{HP} 16 Hz, $PCHCH_AH_B$), and 7.20—7.92 (total 15 H, m, Ph and Ph_2PO); $\nu_{max.}$ 1 735 (CO_2Et), 1 680 (C=O), 1 440 (P–Ph), and 1 195 cm^{-1} (P=O); *m/z* 406 (M^+), 360 [(M − EtOH)$^+$, 42], 333 [(M − CO_2Et)$^+$, 42], and 201 (Ph_2PO^+, 100) (Found: M^+, 406.1338. $C_{24}H_{23}O_4P$ requires M, 406.1334), and a compound tentatively identified as ethyl [1-phenyl-2-(diphenylphosphinoyl)vinyloxy] acetate (8 mg, 2%) as an oil, R_F 0.12 (EtOAc); $\nu_{max.}$ 1 745 (CO_2Et), 1 635 (C=C), 1 440 (P–Ph), and 1 160 cm^{-1} (P=O) (Found: M^+, 406.1336. $C_{24}H_{23}O_4P$ requires M, 406.1334).

3-*Diphenylphosphinoyl*-3-*methylbutan*-2-*one* (12; R^1 = R^2 = R^3 = Me) (*Method B*).—3-(Diphenylphosphinoyl)butan-2-one (3; R^1 = R^2 = Me) (500 mg, 1.84 mmol) was stirred with sodium methoxide (100 mg, 1.84 mmol) and an excess of methyl iodide in dry THF under nitrogen for 2 h. Aqueous NH_4Cl (20 ml) was then added, the layers were separated, the aqueous layer was extracted with chloroform (3 × 25 ml), and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give an off-white solid. P.l.c. on silica (EtOAc) gave the ketone (226 mg, 43%), m.p. 104—106 °C (from EtOAc); R_F 0.22 (EtOAc); δ_H ($CDCl_3$) 1.45 (6 H, d, J_{PH} 14 Hz, CMe_2), 2.25 (3 H, s, MeCO), and 7.50—8.00 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 710 (C=O), 1 440 (P–Ph), and 1 180 cm^{-1} (P=O); *m/z* 286 (M^+, 14%), 271 [(M − Me^+, 10], and 201 (Ph_2PO^+, 100) (Found: M^+, 296.1136. $C_{17}H_{19}O_2P$ requires M, 296.1122).

Ethyl 3-*Diphenylphosphinoyl*-3-*methyl*-4-*oxopentanoate* (23; R = Me) (*Method A*).—The ketone (3; R^1 = R^2 = Me) (1.088 g, 4 mmol) was stirred in dry THF (10 ml) at 0 °C under nitrogen with sodium hydride (210 mg, 4.4 mmol) for 0.5 h, ethyl bromoacetate (0.73 g, 4.4 mmol) was then added dropwise, the mixture was stirred at 0 °C for 2 h and was then warmed to room temperature. Distilled water (20 ml) was added, the layers were separated, the aqueous layer was extracted with EtOAc (3 × 20 ml), and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give an oil. Column chromatography on silica (eluted with EtOAc) gave the keto ester (23; R = Me) (1.152 g, 80%) as an oil, R_F 0.35 (EtOAc); δ_H ($CDCl_3$) 1.22 (3 H, t, J_{HH} 7 Hz, CH_2Me), 1.66 (3 H, d, J_{PH} 15 Hz, PCMe), 2.20 (3 H, s, MeCO), 2.65 (1 H, dd, J_{AB} 17 and J_{PA} 6 Hz, $PCCH_AH_B$), 3.07 (2 H, q, J_{HH} 7 Hz, CH_2Me), 3.53 (1 H, dd, J_{AB} 17 and J_{PB} 7 Hz, $PCCH_AH_B$), and 7.36—8.10 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 730 (CO_2R), 1 695 (C=O), 1 440 (P–Ph), and 1 185 cm^{-1} (P=O); *m/z* 358 (M^+, 0.8%), 312 [(M − EtOH)$^+$, 16], and 201 (Ph_2PO^+, 100) (Found: M^+, 358.1321. $C_{20}O_{23}O_4P$ requires M, 358.1334).

Alkylation of the Ketone (3; R^1 = Me, R^2 = Ph) *with Ethyl Bromoacetate* (*Method A*).—The ketone (3; R^1 = Me, R^2 = Ph) (334 mg, 1 mmol) was stirred with sodium hydride (53 mg, 1.1 mmol) in dry THF (10 ml) for 0.5 h at 0 °C under nitrogen. Ethyl bromoacetate (0.18 g, 1.1 mmol) was added dropwise and the mixture stirred for 6 h at room temperature; it was then poured into aqueous NH_4Cl (20 ml), the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 15 ml). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give an oil. P.l.c. on silica (EtOAc) gave ethyl 3-diphenylphosphinoyl-3-methyl-4-oxo-4-phenylbutanoate (12; R^1 = Me, R^2 = CH_2CO_2Et, R^3 = Ph) (106 mg, 25%) as an oil, R_F 0.49 (EtOAc); δ_H ($CDCl_3$) 0.95 (3 H, t, J_{HH} 7 Hz, CH_2Me), 1.64 (3 H, d, J_{PH} 15 Hz, PCMe), 2.65 (1 H, dd, J_{AB} 17 and J_{PA} 6 Hz, $PCCH_AH_B$), 3.70 (1 H, dd, J_{AB} 17 and J_{PB} 8 Hz, $PCCH_AH_B$), 3.80 (2 H, q, J_{HH} 7 Hz, CH_2Me), and 7.00—8.05 (total 15 H, m, Ph, and Ph_2PO); $\nu_{max.}$ 1 730 (CO_2Et), 1 670 (C=O), 1 435 (P–Ph), and 1 180 cm^{-1} (P=O); *m/z* 420 (M^+, 66%) and 374 [(M − CO_2Et)$^+$, 100] (Found: M^+, 420.1500. $C_{25}H_{25}O_4P$ requires M, 420.1491).

Also obtained was ethyl (2-diphenylphosphinoyl-1-phenylprop-1-enyloxy)acetate (13) (227 mg, 54%) as an oil, R_F 0.13 (EtOAc); δ_H ($CDCl_3$) 1.00 (3 H, t, J_{HH} 7 Hz, CH_2Me), 1.78 (3 H, d, J_{PH} 14 Hz, PCMe), 3.18 (2 H, s, OCH_2), 3.82 (2 H, q, J_{HH} 7 Hz, CH_2Me), and 7.10—7.94 (total 15 H, m, Ph and Ph_2PO); $\nu_{max.}$ 1 755 (CO_2Et), 1 630 (C=C), 1 440 (P–Ph), and 1 140 cm^{-1} (P=O); *m/z* 420 (M^+, 16%), 347 [(M − CO_2Et)$^+$, 24], and 333 [(M − CH_2CO_2Et)$^+$, 100] (Found: M^+, 420.1455. $C_{25}H_{25}O_4P$ requires M, 420.1491).

(E)- *and* (Z)-1-*Diphenylphosphinoylmethylene*-2-*oxacycloheptane* (16).—The hydroxy ketone [2] (14) (330 mg, 1 mmol) was stirred in dry DMF (5 ml) at 0 °C under nitrogen with triphenylphosphine (262 mg, 1 mmol). Bromine was added dropwise at this temperature until the orange colour persisted, and the mixture was then stirred for 0.5 h. Water (100 ml) was added and the mixture was extracted with diethyl ether (4 × 20 ml). The combined ethereal extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a mixture of triphenylphosphine oxide and the crude bromide (15; X = Br), R_F 0.46 (EtOAc); δ_H ($CDCl_3$) 1.10—1.86 (6 H, m, 3 × CH_2), 2.58 (3 H, t, J_{HH} 7 Hz, $COCH_2$),

3.22 (3 H, t, J_{HH} 7 Hz, CH_2O), 3.52 (2 H, d, J_{PH} 15 Hz, PCH_2), and 7.20—7.80 (10 H, m, Ph_2PO).

The crude mixture was stirred with sodium hydride (53 mg, 1.1 mmol) in dry THF (5 ml) at 0 °C under nitrogen for 2 h, and then for 2 d at room temperature. The mixture was then poured into water (100 ml), the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a white solid. P.l.c. on silica (EtOAc) gave triphenylphosphine oxide (243 mg, 87%) together with the *E* and *Z* isomers of the enol ether (16). High-R_F isomer (54 mg, 17%), R_F 0.27 (EtOAc); δ_H ($CDCl_3$) 1.40—1.80 (6 H, m, 3 × CH_2), 2.80 (2.80 (2 H, m, =CHCH_2), 4.04 (2 H, m, OCH_2), 5.10 (1 H, d, J_{PH} 19 Hz, PCH), and 7.24—7.60 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 650 (C=C), 1 435 (P–Ph)

[redacted]

and 1 175 cm^{-1} (P=O); *m/z* 313 [$(M + 1)^+$, 2%], 312 (M^+, 0.4), 202 [$Ph_2P(O)H^+$, 55], and 201 (Ph_2PO^+, 100) (Found: M^+, 312.1260. $C_{19}H_{21}O_2P$ requires *M*, 312.1279).

Low-R_F isomer (61 mg, 20%), R_F 0.08 (EtOAc), δ_H ($CDCl_3$) 1.40—1.70 (6 H, m, 3 × CH_2), 2.44 (2 H, m, =CHCH_2), 3.76 (2 H, m, OCH_2), 4.86 (1 H, d, J_{PH} 15 Hz, PCH), and 7.20—7.80 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 655 (C=C), 1 440 (P–Ph), and 1 170 cm^{-1} (P=O); *m/z* 313 [$(M + 1)^+$, 11%], 312 (M^+, 1.5), 202 [$Ph_2P(O)H^+$, 55], and 201 (Ph_2PO^+, 100) (Found: M^+, 312.1292. $C_{19}H_{21}O_2P$ requires *M*, 312.1279).

7-Diphenylphosphinoyl-6-oxoheptyl Toluene-p-sulphonate (15; X = OTs).—The hydroxy ketone (14) (330 mg, 1 mmol) was heated under reflux with toluene-*p*-sulphonic acid (190 mg, 1 mmol) in benzene (20 ml) in a Dean–Stark apparatus for 7 d under nitrogen. The solution was then cooled, washed with saturated aqueous sodium hydrogen carbonate (3 × 50 ml), dried ($MgSO_4$), and evaporated under reduced pressure to give an oil. P.l.c. on silica (EtOAc) gave the tosylate (416 mg, 86%) as an oil, R_F 0.5 (EtOAc); δ_H ($CDCl_3$) 1.00—1.70 (6 H, m, 3 × CH_2), 2.38 (3 H, s, Ar*Me*), 2.60 (2 H, t, J_{HH} 6 Hz, $COCH_2[CH_2]_4$), 3.58 (2 H, d, J_{PH} 14 Hz, PCH_2),

nitrogen for 15 min. Methyl acrylate (130 mg, 1.5 mmol) was then added, the solution was stirred for a further 2 h at room temperature and then poured into aqueous NH_4Cl (20 ml). The layers were separated, the aqueous layer was extracted with $CHCl_3$ (3 × 20 ml), and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the dione (18) (270 mg, 55%), m.p. 208—211 °C (from $CHCl_3$); R_F 0.05 (EtOAc); δ_H (CF_3CO_2D) 1.8 (3 H, d, J_{PH} 16 Hz, PCMe), 2.0—3.1 (4 H, m, 2 × ring CH_2), and 7.6—8.2 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 640 (C=O), 1 600 (C=C), 1 440 (P–Ph), and 1 190 cm^{-1} (P=O); *m/z* 326 (M^+, 57%) and 201 (Ph_2PO^+, 100) (Found: M^+, 326.1066. $C_{19}H_{19}O_3P$ requires *M*, 326.1072.

Attempted Reaction of 1-(Diphenylphosphinoyl)propan-2-one with Pent-3-en-2-one.—1-(Diphenylphosphinoyl)propan-2-one (11; R^2 = Me) (258 mg, 1 mmol) was stirred with sodium hydride (55 mg, 1.15 mmol) in dry THF (5 ml) at room temperature under nitrogen for 0.5 h. Pent-3-en-2-one (92 mg, 1.1 mmol) was then added and the solution was stirred for 48 h at room temperature. Aqueous NH_4Cl (20 ml) was then added, the layers were separated, the aqueous layer was extracted with EtOAc (3 × 20 ml), and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give an orange oil. P.l.c. on silica (EtOAc) gave only recovered starting material (245 mg, 95% recovery).

1-(Diphenylphosphinoyl)butan-2-one (3; R^1 = H, R^2 = Et) *by Methylation of the Dianion of 1-(Diphenylphosphinoyl)-propan-2-one.*—The ketone (11; R^2 = Me) (516 mg, 2 mmol) was stirred with sodium hydride (110 mg, 2.3 mmol) in dry THF (10 ml) under nitrogen at 0 °C for 15 min. The pale-yellow solution was cooled to −78 °C, BuLi (1.5 ml, 2.3 mmol) was added, and the deep-red solution was stirred for 5 min. Methyl iodide (0.33 g, 2.3 mmol) was then added dropwise during 2 min. The mixture was allowed to warm to room temperature, aqueous NH_4Cl (20 ml) was added, the layers

mmol) was dissolved in methanol (10 ml) containing four drops of 10% aqueous sodium hydroxide. Sodium borohydride (40 mg, 1.05 mmol) was then added and the solution was stirred at room temperature under nitrogen for 24 h. After *careful* destruction of any residual borohydride with dilute hydrochloric acid, the methanol was removed under reduced pressure and the aqueous layer was extracted with EtOAc (4 × 20 ml). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (2 × 20 ml) dried (Na_2SO_4), and evaporated under reduced pressure to give a white solid. P.l.c. on silica (EtOAc) gave the *lactone* (24; R = H) (260 mg, 92%) as an inseparable 3 : 1 mixture of diastereoisomers, m.p. 155—158 °C (from EtOAc) (Found: C, 68.3; H, 5.85%; M^+, 300.0919. $C_{17}H_{17}O_3P$ requires C, 68.0; H, 5.70%; *M*, 300.0915). *Major isomer*: R_F 0.36 (EtOAc); δ_H ($CDCl_3$) 1.44 (3 H, d, J_{HH} 7 Hz, Me), 2.42 (1 H, ddd, J_{HA} 8, J_{AB} 17, and J_{PA} 2.5 Hz, $COCH_AH_B$), 3.28 (1 H, dd, J_{AB} 17 and J_{PB} 13 Hz, $COCH_AH_B$), 3.60 (1 H, m, PCH), 4.86 (1 H, m, J_{PH} *ca.* 2.5 Hz, MeC*H*), and 7.36—8.00 (10 H, m, Ph_2PO). *Minor isomer*: R_F 0.36 (EtOAc); δ_H ($CDCl_3$) 1.12 (3 H, d, J_{HH} 7 Hz, Me), 2.60—3.20 (2 H, m, $COCH_AH_B$), 3.60 (1 H, m, PCH), 4.90 (1 H, m, MeC*H*), and 7.36—8.00 (10 H, m, Ph_2PO). (Mixture): $\nu_{max.}$ 1 770 (C=O), 1 440 (P–Ph), and 1 180 cm^{-1} (P=O); *m/e* 300 (M^+, 11%), 202 [$Ph_2P(O)H^+$, 80], and 201 (Ph_2PO^+, 100).

4-Diphenylphosphinoyl-4,5-dihydro-4,5-dimethylfuran-2(3H)-one (24; R = Me).—The keto ester (23; R = Me) (300 mg, 0.84 mmol) was dissolved in methanol (10 ml) containing four drops of 10% aqueous sodium hydroxide. Sodium borohydride (35 mg, 0.93 mmol) was then added and the solution was stirred at room temperature under nitrogen for 24 h. Identical work-up as for compound (24; R = H) gave an oil. P.l.c. on silica (EtOAc) gave the oily *lactone* (24; R = Me) (215 mg, 82%) as an inseparable 5 : 3 mixture of diasteroisomers. Major isomer: R_F 0.33 (EtOAc); δ_H ($CDCl_3$) 1.40 (3 H, d, J_{PH} 15 Hz, PCMe), 1.45 (3 H, d, J_{HH} 7 Hz, *Me*CHO), 2.28 (1 H, d, J_{AB} 17 and J_{PA} 2.5 Hz, $PCCH_AH_B$), 3.72 (1 H, dd, J_{AB} 17 and J_{PB} 11 Hz, $PCCH_AH_B$), 4.64 (1 H, dq, J_{HH} 7 and J_{PH} 2.5 Hz, MeC*H*O), and 7.40—8.06 (10 H, m, Ph_2PO). Minor isomer: R_F 0.33 (EtOAc); δ_H ($CDCl_3$) 1.18 (3 H, d, J_{HH} 7 Hz, *Me*CHO), 1.35 (3 H, d, J_{PH} 15 Hz, PCMe), 2.44 (1 H, dd, J_{AB} 17 and J_{PA} 2.5 Hz, $PCCH_AH_B$), 3.38 (1 H, dd, J_{AB} 17 and J_{PB} 13 Hz, $PCCH_AH_B$), 5.03 (1 H, dq, J_{HH} 7 and J_{PH} 9 Hz, MeC*H*O), 7.40—8.06 (10 H, m, Ph_2PO). (Mixture): $\nu_{max.}$ 1 770 (C=O), 1 440 (P–Ph), and 1 185 cm^{-1} (P=O); *m/z* 314 (M^+, 8%), 219 [$Ph_2P(O)_2H_2^+$, 100], and 201 (Ph_2PO^+, 79) (Found: M^+, 314.1068. $C_{18}H_{19}O_3P$ requires *M*, 314.1072).

Butyl 4-Diphenylphosphinoyl-3-methylpent-2-enoate (32; Z = Ph_2PO).—The lactone (24; R = Me) (100 mg, 0.32 mmol) was heated under reflux with toluene-*p*-sulphonic acid (70 mg, 0.37 mmol) in a mixture of chlorobenzene (5 ml) and n-butyl alcohol (5 ml) under nitrogen for three weeks. The mixture was then cooled, washed with saturated aqueous sodium hydrogen carbonate (3 × 25 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give an orange oil. P.l.c. on silica (EtOAc) gave recovered lactone (24; R = Me) (9 mg, 8% recovery), together with the rearranged ester (32; Z = Ph_2PO) (5 mg, 4%) as an oil, R_F 0.55 (EtOAc); δ_H ($CDCl_3$) 0.70—1.70 (total 7 H, m, CH_2CH_2Me), 1.35 (3 H, dd, J_{HH} 9 and J_{PH} 20 Hz, PCH*Me*), 2.10 (3 H, br s, =CMe), 3.05 (1 H, m, PC*H*Me), 3.95 (2 H, t, J_{HH} 8 Hz, OCH_2), 5.65 (1 H, br s, =CH), and 7.30—7.94 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 720 (CO_2Bu), 1 445 (P–Ph), and 1 185 cm^{-1} (P=O); *m/z* 370 (M^+, 100%), 297 [$(M - OBu)^+$, 34], and 269 [$(M - CO_2Bu)^+$, 28) (Found: M^+, 370.1709. $C_{22}H_{27}O_3P$ requires *M*, 370.1698).

Acknowledgement

We thank S.E.R.C. for a grant (to R. S. T.).

References

1 A. D. Buss and S. Warren, *J. Chem. Soc., Chem. Commun.*, 1981, 100.
2 R. S. Torr and S. Warren, *J. Chem. Soc. Pak.*, 1979, **1**, 15.
3 W. G. Dauben, G. H. Beasley, M. D. Broadhurst, B. Muller, D. J. Peppard, P. Pesnelle, and C. Suter, *J. Am. Chem. Soc.*, 1975, **97**, 4973.
4 W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.*, 1961, **83**, 1733; J. Boutagy and R. Thomas, *Chem. Rev.*, 1974, **74**, 87.
5 N. A. Portnoy, C. J. Morrow, M. S. Chatta, J. C. Williams, and A. M. Aguiar, *Tetrahedron Lett.*, 1971, 1397, 1401; see also N. A. Portnoy, K. S. Yong, and A. M. Aguiar, *ibid.*, p. 2559.
6 J. E. Baldwin and L. I. Kruse, *J. Chem. Soc., Chem. Commun.*, 1977, 233.
7 P. Brownbridge, E. Egert, P. G. Hunt, O. Kennard, and S. Warren, *J. Chem. Soc., Perkin Trans. I*, 1981, 2751.
8 C. Benezra, *J. Am. Chem. Soc.*, 1973, **95**, 6890.
9 M. Chérest, H. Felkin, and N. Prudent, *Tetrahedron Lett.*, 1968, 2199.
10 P. Brownbridge and S. Warren, *J. Chem. Soc., Chem. Commun.*, 1977, 465.
11 I. J. Borowitz and R. K. Crouch, *Phosphorus*, 1973, **2**, 209.

Received 8th November 1982; *Paper* 2/1869