Synthesis of β-(Diphenylphosphinoyl) Ketones

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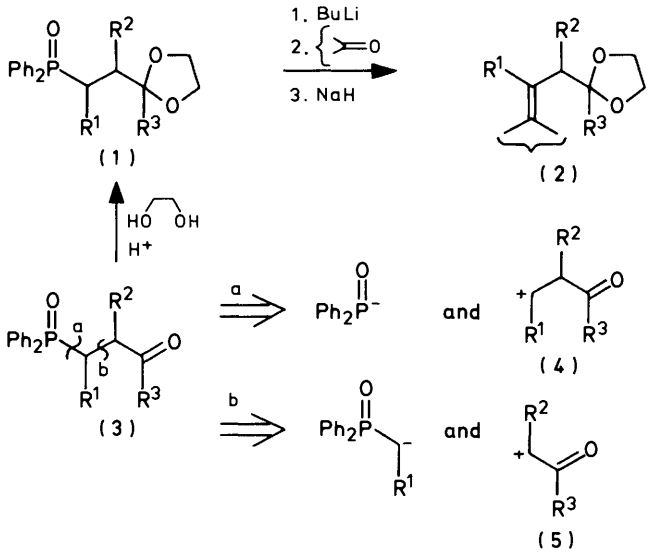
The title compounds may be made by addition of phosphorus nucleophiles (Ph_2PO^-, Ph_2POMgX, Ph_2PCl) to enones, by addition of phosphorus-stabilised carbanions to α-carbonyl cation equivalents (2,3-dichloropropene, epoxides, and α-MeO-ketones) and by oxidation of allyl diphenylphosphine oxides.

Anions of protected β-(diphenylphosphinoyl)-ketones (1) react [1] as homoenolate equivalents with aldehydes and ketones to give protected β,γ-unsaturated ketones (2). In this paper we describe the synthesis of the starting materials (3) by three versions of strategy (a), in which a diphenylphosphinoyl group adds to the electrophilic carbon framework, (4) and by six versions of strategy (b) in which a phosphorus-stabilised carbanion adds to an α-carbonyl cation (5) equivalent. These nine methods provide routes to most substitution patterns of (3) (Scheme 1).



Scheme 1.

Addition of the Diphenylphosphinoyl Group to the Carbon Framework.—The simplest way to make alkyldiphenylphosphine oxides is usually by alkaline hydrolysis of the corresponding phosphonium salt.[2,3] This is an attractive method to make ketals (8) with a substituent † R^2 directly from keto esters (6) and gives a moderate yield (46%) of (8; R^2 = H) from (7; R^2 = H) but when R^2 = Me) the yield drops to 12%. The problem seems to be steric hindrance in the displacement reactions (Scheme 2).

Better results come from the addition of diphenylphosphinoyl nucleophiles to enones. The anion of diphenylphosphine oxide (9) adds [4] to enones to give ketones of the substitution pattern (3; R^2 = H) in reasonable yield. To avoid the tedious preparation [5] of (9), the Grignard reagent [6] (11) may be added to cyclohexanone, again in reasonable yield (Scheme 3).

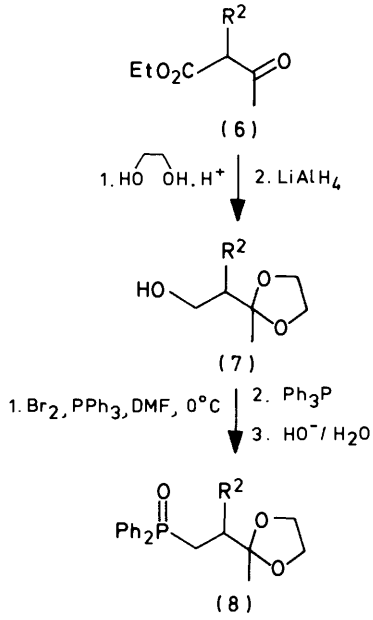
The most general method based on this strategy is the addition of diphenylphosphinous chloride (13) to enones in acetic acid. Conant [7] reported this reaction with R^1 = R^2 = aryl but it also gives reasonable yields (Table 1) with aliphatic enones and unsaturated esters under the right conditions. The mechanism of this reaction probably involves formation of (9) and acetyl chloride from (13) and acetic acid followed by Michael addition of (9) to the enone (Scheme 4).[8]

† R^1, R^2, and R^3 refer to substituents on the same three carbon atoms as in (1), throughout.

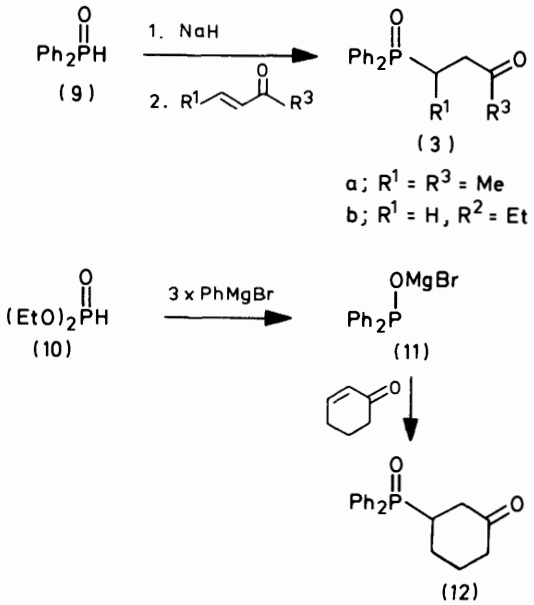
Table 1. Ketones (3; R^2 = H) from addition of diphenylphosphinoyl nucleophiles to enones

Compound	Method [a]	R^1	R^3	Yield (%)
(3a)	A	Me	Me	73
(3a)	B	Me	Me	66 [b]
(3b)	A	H	Et	55
(3b)	B	H	Et	71
(3c)	B	Ph	Ph	88 [c]
(3d)	B	$(CH_2)_3$		66 [d]
(3d)	C	$(CH_2)_3$		62 [d]
(3e)	B	H	OMe	51
(3f)	B	Me	OEt	55

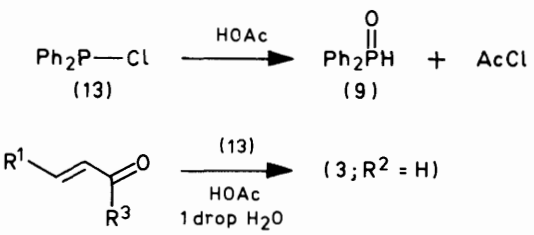
[a] Method A: addition of anion of (9) (NaH); Method B: Conant reaction; Method C: addition of Grignard reagent (11). [b] 53% In acetonitrile. [c] *Cf.* Ref. 7. [d] Product is (12).



Scheme 2.



Scheme 3.



Scheme 4.

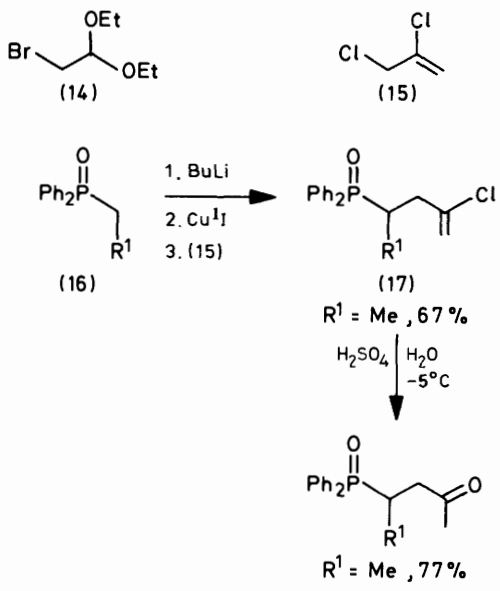
Addition of α-Acyl Cation Equivalents to Phosphorus-stabilised Carbanions.—Alkylation of phosphine oxides (16) with alkyl halides is usually reliable [3,9] and succeeds [10] with the α-bromoacetal (14) and (16; R^1 = Me). Savignac [11] has already reported the reaction of the α-acyl cation equivalent (15) with copper derivatives of phosphonate esters and this method was successful with the phosphine oxide (16; R^1 = Me) (Scheme 5).

Horner [12] has reported the addition of (16; R^1 = Ph) to styrene oxide (18) (though he gave probably the wrong structure for the product [13]) using phenyl-lithium in ether to generate the carbanion. We find that anions from (16; R^1 = Me) and butyl-lithium in tetrahydrofuran (THF) give only regioisomer (19) in good yield. Cyclohexene oxide (21) also adds to these anions to give (22) as reported by Horner.[12] Alcohols (19) and (22) may be oxidised to ketones (20) and (23) by Jones's reagent,[14] pyridinium dichromate,[15] or sodium hypochlorite in acetic acid.[16,17] It is not necessary to isolate and purify the alcohols (19) or (22): this is an advantage if a mixture of diastereoisomers occurs at this stage.* This method clearly requires that the regioselectivity of epoxide opening can be controlled.

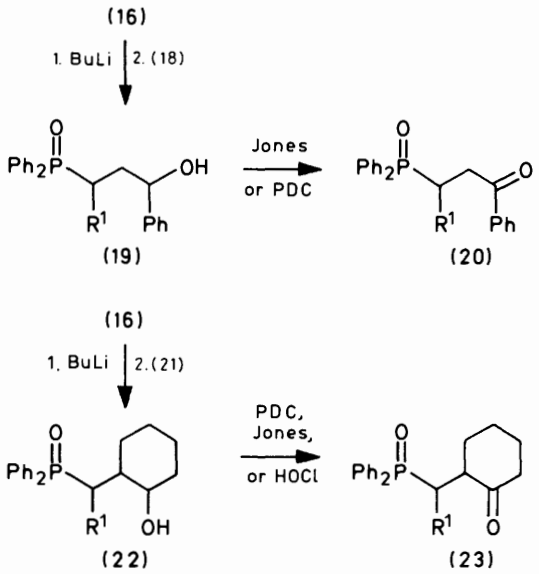
Addition of Phosphorus-stabilised Anions to α-Methoxy Ketones.—Ketones with a good leaving group on an α-carbon atom are α-carbonyl cation (5) equivalents: α-methoxy ketones become so after alkylative [1,2] carbonyl transposition [18] (Scheme 7). This route can give ketones (28) with all three substituents R^1, R^2, and R^3, though R^2 must be methyl if the α-methoxy ketones are made by the hydration of (24), conveniently available [19] from adducts of acetylene and R^3-CHO.

Addition of anions from (16) (BuLi, THF) to (25) gives alcohols (26). Such tertiary alcohols usually dehydrate readily in trifluoroacetic acid (TFA) to give allyl phosphine oxides with the double bond in the more highly substituted side chain.[3] This regioselectivity in the dehydration of (26) gives vinyl ethers (27) which are hydrolysed during the aqueous work-up to give ketones (28) (Table 2).

Intermediate (26) and product (28) are usually formed as mixtures of diastereoisomers, though there is some stereoselectivity. Thus (26; R^1 = R^3 = Me) was formed as a (3 : 2)



Scheme 5.



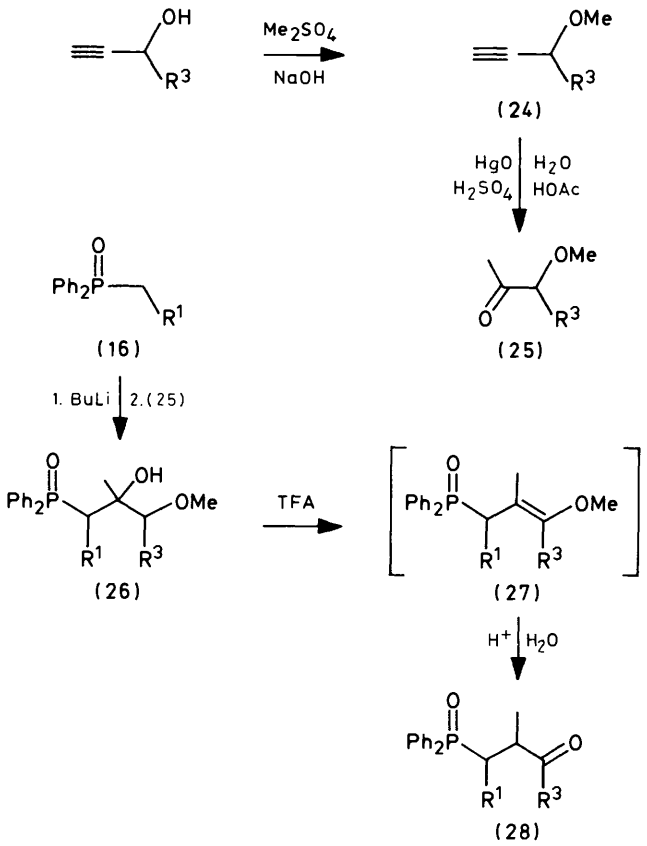
Scheme 6.

* We are exploring the stereoselectivity of (16)—(22) (R^1 = Me) in connection with another project; D. Levin and S. Warren, unpublished observations.

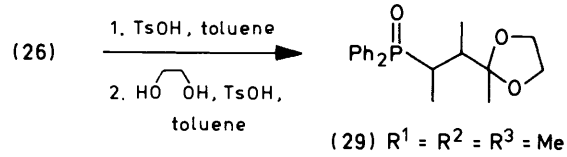
Table 2. Ketones (3) from (16) and α-acyl cation equivalents

Compound	Method [a]	R^1	R^2		R^3	Yield of intermediates (%)	Yield of ketone (%)
(3a)	D	Me	H		Me	(17) 67%	77
(3g)	E	H	H		Ph	(19) 96	97
(3h)	E	Me	H		Ph	(19) 65	61
(3i)	E	H		$(CH_2)_4$		(18) [b]	70 [c]
(3j)	F	H	Me		Me	(26) 88	69
(3j)	G	H	Me		Me	(38j) 64	92 (TFA) 52 (TsOH)
(3k)	F	Me	Me		Me	(26) 75	80
(3l)	F	Et	Me		Me	(26) 52	59

[a] Method D: 2,3-dichloropropene (15); E: Addition of epoxide to (16) and oxidation; F: α-MeO ketone transposition; G: Rearrangement of epoxide of allyl phosphine oxide. [b] See ref. 12. [c] Yield direct from (11).

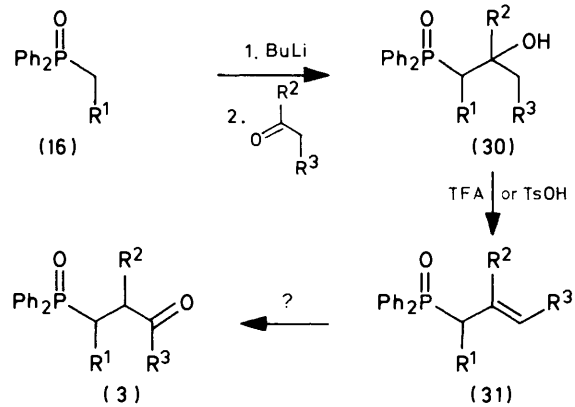


Scheme 7. The α-methoxy ketone route



Scheme 8.

sis [3,9] of allyl phosphine oxides (31) from tertiary alcohols (30) makes them attractive precursors to ketones with substituents on all three carbon atoms (3). This route also involves a carbonyl transposition and requires oxidation at the less-substituted end of the double bond in (31) (Scheme 9).



Scheme 9.

mixture of two of the possible diastereoisomers. The stereoselectivity of additions of anions of (15) to ketones has been studied,[20] but is irrelevant here as one chiral centre (bearing R^3) disappears during the transposition step (26) to (28), another (bearing R^2) is epimerised during this same reaction, and the third (bearing R^1) is epimerised when the ketals (29) are used in β,γ-unsaturated ketone synthesis.[1,21]

The tertiary alcohols (26) may be converted into ketals (29) without isolating ketone (28) if toluene-*p*-sulphonic acid (TsOH) in toluene under reflux replaces TFA in the dehydration step. In the one case examined ($R^1 = R^3 = Me$), the yield was considerably improved, 85% of (29) being obtained in the one step method from (26) (Scheme 8).

Routes from Allyl Phosphine Oxides.—The simple synthe-

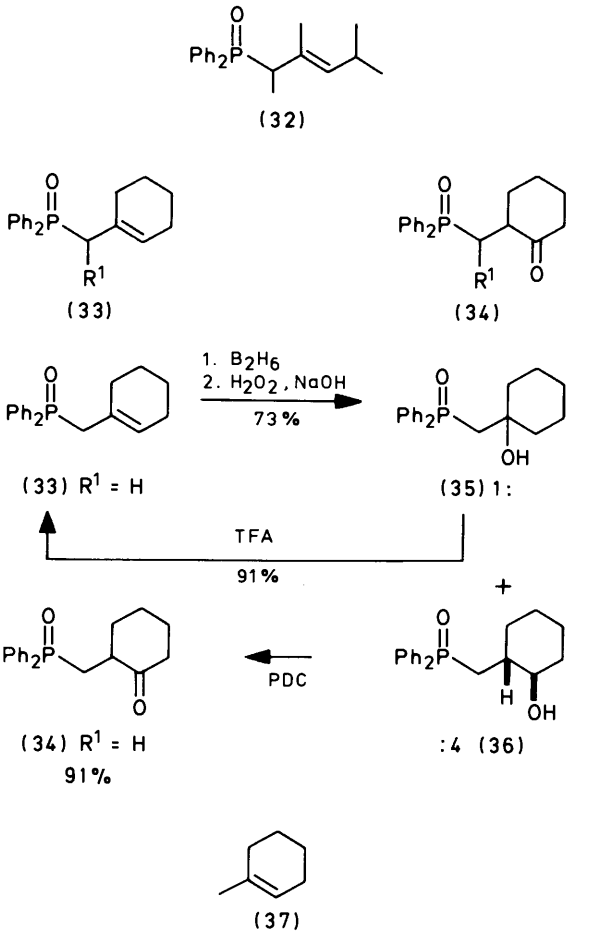
Allyl phosphine oxides resist oxidation. Neither (32) nor (33) reacted with potassium permanganate under a variety of conditions, though (33) is cleaved by ozone.[17] Attempts to convert (33; $R^1 = H$) into the corresponding diol failed, but the direct formation of (34) with iodine and silver acetate did occur, though in low yield. After three weeks with these reagents in acetic acid under reflux, 30% of (34) was formed and 45% of (33; $R^1 = H$) was recovered.

Hydroboration of (33; $R^1 = H$) gave a 1 : 4 ratio of alcohols (35) and (36) in 73% yield. This is a reasonable route to (34; $R^1 = H$) as the alcohols are easily separated, (36) is oxidised to (34; $R^1 = H$) in high yield by PDC, and (35) is an intermediate in the synthesis [22] of (33; $R^1 = H$). Regioselectivity in the hydroboration of (33; $R^1 = H$) is low (4 : 1) compared with that of (37) (24 : 1 in favour of the secondary alcohol [23]) presumably because of the electron-withdrawing effect of the diphenylphosphinoyl group.[24]

Table 3. Epoxides from allyl phosphine oxides

Compound	R^1	R^2	R^3	Yields (38) (%)
(38i)	H	$(CH_2)_4$		91 [b,22]
(38j)	H	Me	Me	64 [a]
(38m)	H	Me	Pr^i	97 [b]
(38n)	Me	Me	Pr^i	86 [b]
(38o)	H	Me	Bu^n	66 [a]
(38p)	Me	Et	Me	79 [a]
(38q)	H	$(CH_2)_3$		92 [b]
(38r)	H	$(CH_2)_5$		97 [b]

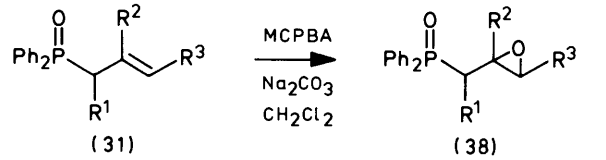
[a] From (16). [b] From (31).



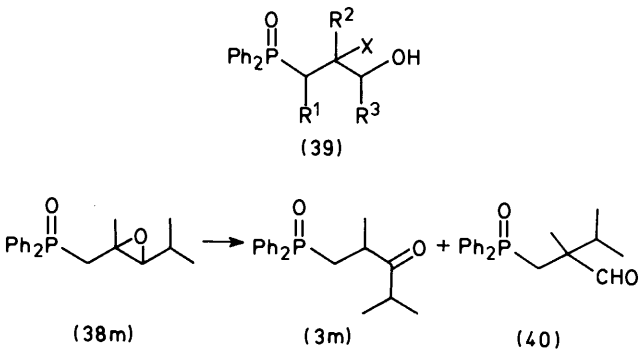
Scheme 10.

Epoxides of Allyl Phosphine Oxides.—Alone among the oxidising agents tried, peracids gave consistently good results with allyl phosphine oxides. *m*-Chloroperbenzoic acid (MCPBA) and sodium carbonate in dichloromethane gave high yields of epoxides (38) from a variety of allyl phosphine oxides (31) (Table 3). The alkyl phosphine oxides (16) can be converted into epoxides (38) without isolating and purifying intermediates (30) and (31): the entire reaction sequence is quick and high yielding and we have already reported some reactions of one epoxide (Scheme 11).[22]

Among many attempts to rearrange epoxides (38) into ketones (3), treatment with Lewis acids (boron trifluoride–ether, lithium perchlorate, lithium bromide, titanium tetrachloride or magnesium bromide) gave no reaction or mixtures of products in which epoxide (38), ketone (3), and the substitution products (39; X = Cl, Br) could be detected (Scheme 12).



Scheme 11.



Scheme 12.

Protic acids gave better results, and TFA was generally the best of these. Thus (38m), which gave a mixture of unidentified products with HCl or TsOH, gave ketone (3m) and aldehyde (40) with TFA. Epoxide (38p) also gave some of the required ketone with TFA and (38j) gave an excellent yield of (3j). However, the reaction was capricious and failed with most epoxides. The diphenylphosphinoyl group appears to destabilise * tertiary cation (41) in the same way as it reduced the regioselectivity of hydroboration of (33; R^1 = H). Aldehyde (40) is presumably formed from (41) by R^3 migration (Scheme 13).

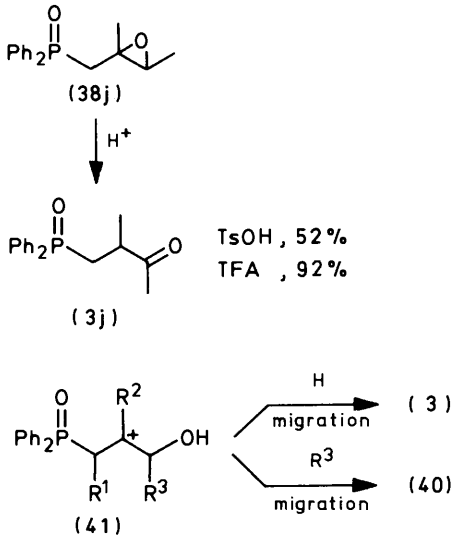
A survey of the available methods for the synthesis of (34; R^1 = H) is given in Table 4. The best epoxide rearrangement is again with TFA which gives 30% of (3i) and 50% of diol (42) which could be converted into (3i) with TFA at a higher temperature in 60% yield. However, no epoxide rearrangement can match hydroboration, and the alternative route using the addition of cyclohexene oxide (21) to the anion of methyl diphenylphosphine oxide (16; R^1 = H) gives easily the best yield.

Application.—We have used the products of these reactions in syntheses of β,γ-unsaturated ketones.[1,21] The most useful syntheses for this purpose were the Conant reaction and the addition of phosphorus-stabilised anions to epoxides. These are most useful because they are the most reliable over a variety of structural types.

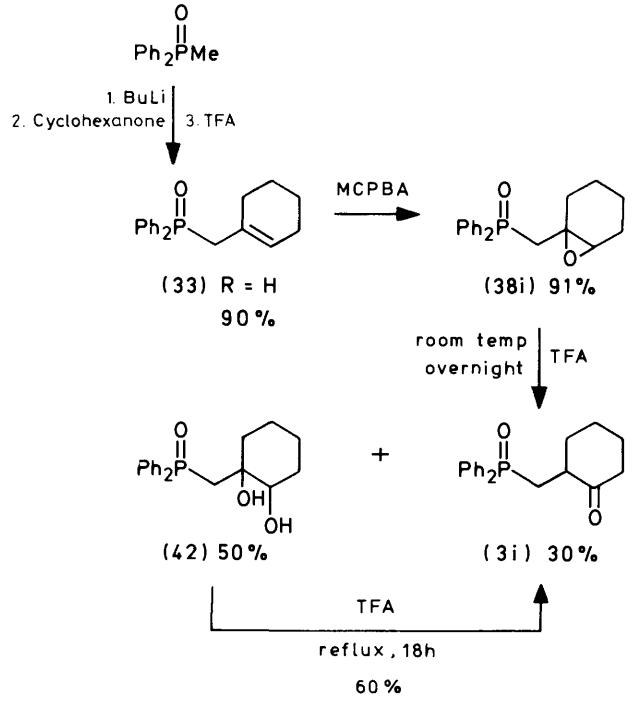
Experimental

I.r. spectra were taken on a Perkin-Elmer 257 or 297, n.m.r. spectra on Varian Associates HA100D, EM 360A, Hitachi

* Yet (26) to (28) must occur *via* a very similar intermediate.



Scheme 13.



Scheme 14.

Perkin-Elmer R24B or CFT20, and mass spectra on A.E.I. MS9, MS30, or MS902 machines. Thin (t.l.c.) and preparative (p.l.c.) layer chromatography were run on silica gel GF_{254} and column chromatography on Merck silica Kieselgel 60, eluted with ethyl acetate (EtOAc) and R_F values given for development in EtOAc unless otherwise stated. M.p.s were taken on a Kofler or a Reichert hot-stage apparatus. TsOH refers to toluene-*p*-sulphonic acid monohydrate, TFA to trifluoroacetic acid, THF to tetrahydrofuran distilled from lithium aluminium hydride immediately before use, MCPBA to *m*-chloroperbenzoic acid, and DMF to dimethylformamide. Diastereotopic groups of protons are marked with an asterisk.

4-*Diphenylphosphinoylbutan-2-one Ethylene Acetal* (8; R^2 = H).—The alcohol (7; R^2 = H) [25] (2 g, 15.2 mmol) and triphenylphosphine (4 g, 15.2 mmol) were dissolved in dry DMF (20 ml) at 0 °C and under nitrogen. Bromine was added dropwise with vigorous stirring at 0 °C until a faint orange colour persisted—then the solution was stirred for a further 0.25 h at 0 °C. Dry benzene (40 ml) and triphenylphosphine (4 g, 15.2 mmol) were added and the solution heated under reflux, under nitrogen, for 1.5 h. After cooling, the mixture was poured into water (250 ml) and extracted with chloroform (5 × 50 ml). The combined organic extracts were dried (K_2CO_3) and evaporated under reduced pressure to give an oil. Sodium hydroxide solution (100 ml, 10%) was added and the mixture distilled until all the benzene had been removed. The residue was cooled and extracted with EtOAc (3 × 50 ml). The combined organic layers were washed with water (2 × 50 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give a white solid. Column chromatography on silica (eluted with EtOAc), gave triphenylphosphine oxide (3.87 g, 91%), and the *phosphine oxide* (8; R^2 = H) (2.21 g, 46%) as needles, m.p. 100—101 °C (from EtOAc) (Found: C, 68.1; H, 6.70; P, 9.9. $C_{18}H_{21}O_3P$ requires C, 68.3; H, 6.70; P, 9.8%), R_F 0.16 (EtOAc), δ ($CDCl_3$) 1.30 (3 H, s, Me), 2.00, m, PCH_2CH_2), 2.40 (2 H, m, PCH_2CH_2), 3.88 (4 H, m, OCH_2-CH_2O), and 7.30—7.80 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 435 (P—Ph) and 1 180 cm^{-1} (P=O); *m/z* 316 (M^+, 1.8%), 301 (*M* — Me, 10), 202 (Ph_2POH^+, 100), and 201 (Ph_2PO^+, 45) (Found: M^+, 316.1210. $C_{18}H_{21}O_3P$ requires *M*, 316.1229).

Ethyl 2-Methyl-3-oxobutanoate Ethylene Acetal.—Ethyl 2-methyl-3-oxobutanoate (6; R^2 = Me) (43 g), ethylene glycol (16.1 g), and TsOH (0.13 g) were heated under reflux in toluene (100 ml); water was removed with a Dean-Stark trap. After 90 min, 5.8 ml of water had collected. The solution was cooled, washed with 2M-sodium hydroxide (20 ml) and water (4 × 20 ml), dried (K_2CO_3), and distilled to give the acetal (49.4 g, 84%), b.p. 65—68 °C/0.9 mmHg, of sufficient purity

Table 4. Synthesis of (3i) from (16; R^1 = H)

From allylphosphine oxide (33; R^1 = H) [90% from (16; R^1 = HK] [22]

	% Yield (3i)	Other products, % yield	% Yield (3i) from (16)
(a) Direct			
1 I_2, AgOAc, HOAc 3 weeks, reflux	30	(30; R = H), 45	27
(b) *Via* Epoxide (38i) [91% from (33; R^1 = H)]			
2 TsOH, PhH, 25 °C	0	(38i), 100	0
3 TsOH, PhH, reflux	40	Unidentified	32
4 BF_3, Et_2O	40	Unidentified	32
5 TFA, overnight, 25 °C	30	Diol (42) 50	49 [a]
(c) Hydroboration			
6 i B_2H_6 ii H_2O_2, NaOH iii Jones	58	Alcohol (35) 14	66 [b]
By cyclohexene oxide addition to (16; R^1 = H)			
7 (16; R^1 = H) → (22; R^1 = H) → (3i)			70

[a] Including conversion of (42) into (3i), see text. [b] Including one recycling of alcohol (35), see text.

for the next stage. It had δ ($CDCl_3$) 1.25 (3 H, t, *J* 7 Hz, OCH_2CH_3), 1.31 (3 H, d, *J* 7 Hz, CH*Me*), 1.38 (3 H, s, CMe), 2.72 (1 H, q, *J* 7 Hz, C*H*Me), 3.89 (4 H, s, OCH_2CH_2O), and 4.08 (2 H, q, *J* 7 Hz, OCH_2CH_3).

4-*Hydroxy*-3-*methylbutan*-2-*one Ethylene Acetal* (7; R^2 = Me).—The above ester (9.4 g) in dry ether (20 ml) was reduced with lithium aluminium hydride (1.14 g) in ether (80 ml) by the method of Fieser.[26] Distillation gave the hydroxy acetal (7; R^2 = Me) (5.3 g, 73%), b.p. 56—61 °C/0.5 mmHg, pure enough for the next stage. It had δ ($CDCl_3$) 0.96 (3 H, d, *J* 7 Hz, CH*Me*), 1.3 (3 H, s, CMe), 2.0 (1 H, m, C*H*Me), 2.9 (1 H, br OH), 3.6 (2 H, m, CH_2OH), and 3.95 (4 H, s, OCH_2CH_2O).

4-*Diphenylphosphinoyl*-3-*methylbutan*-2-*one Ethylene Acetal* (8; R^2 = Me).—The method described above from hydroxy acetal (7; R^2 = Me) (1.6 g) gave crystals, identified as phosphine oxide (8; R^2 = Me) (0.4 g, 12%) from its n.m.r. spectrum. It had δ ($CDCl_3$) 1.09 (3 H, d, *J* 6 Hz, CH*Me*), 1.21 (3 H, s, CMe), 2.2 (1 H, m, C*H*Me), 2.6 (2 H, m, PCH_2), 3.8 (4 H, m, OCH_2CH_2O), and 7.3—8.0 (10 H, m, Ph_2PO).

2-*Diphenylphosphinoylpentan*-4-*one* (3a): *Method A*.—Diphenylphosphine oxide [5] (5 g) and pent-3-en-2-one (2.1 g, 2.5 ml) were dissolved in dry THF (20 ml). Sodium hydride (125 mg of a 50% dispersion in oil) was added and the mixture stirred at room temperature for 3 h. Concentrated hydrochloric acid (0.25 ml) was added dropwise, the mixture filtered, and the filtrate evaporated to give a gum. Column chromatography (EtOAc–5% MeOH) gave the *ketone* (3a) (5.2 g, 73%), m.p. 100—102 °C, R_F 0.24, δ 1.1 (3 H, dd, J_{HH}, *J* 7, J_{PH} 16 Hz, PCH*Me*), 2.03 (3 H, s, COMe), 2.63 (2 H, t, J_{HH} = J_{HP} 9 Hz, CH_2CO) 3.3—2.9 (1 H, m, PCH), and 7.2—8.0 (10 H, m, Ph_2PO) (Found: C, 71.3; H, 6.6; P, 10.7. $C_{17}H_{19}O_2P$ requires C, 71.3; H, 6.7; P, 10.8%), $\nu_{max.}$ 1 715 (C=O), 1 435 (P–Ph), and 1 200 cm^{-1} (P=O); *m*/*z* 286 (M^+, 24%), 271 (*M* − Me, 3), 202 (Ph_2POH^+, 100), and 201 (Ph_2PO^+, 77) (Found: M^+, 286.1130. $C_{17}H_{19}O_2P$ requires *M*, 286.1122).

1-*Diphenylphosphinoylpentan*-3-*one* (3b).—By method A, diphenylphosphine oxide (5 g), ethyl vinyl ketone (2.1 g, 2.5 ml), and sodium hydride (125 mg of a 50% dispersion in oil) gave, after column chromatography (ethyl acetate–3% methanol), the *ketone* (3b) (3.9 g, 55%) as a colourless gum, R_F 0.25, δ ($CDCl_3$) 1.02 (3 H, t, *J* 7 Hz, CH_2Me), 2.39 (2 H, q, *J* 7 Hz, CH_2Me), 2.2—3.0 (4 H, m, PCH_2CH_2), and 7.2—8.0 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 710 (C=O), 1 440 (P–Ph), and 1 185 cm^{-1} (P=O); *m*/*z* 286 (M^+, 6%), 257 (*M* − Et, 38), 202 (Ph_2POH^+, 100), and 201 (Ph_2PO^+, 40) (Found: M^+, 296.1121. $C_{17}H_{10}O_2P$ requires *M*, 286.1123).

3-*Diphenylphosphinoyl*-1,3-*diphenylpropan*-1-*one* (3c): *Method B*.—A solution of 1,3-diphenylpropenone (2.3 g, 11 mmol) in glacial acetic acid (10 ml) was added dropwise, with vigorous stirring, to diphenylphosphinous chloride (2.2 g, 10 mmol), at room temperature and under nitrogen, over a period of 5 min. Then 5 drops of distilled water were added and the solution heated under reflux, under nitrogen, for 2 h; it was then cooled and poured into water (100 ml) to give a thick white precipitate. The mixture was extracted with chloroform (5 × 50 ml), and the combined organic layers dried (Na_2SO_4) and evaporated under reduced pressure to give a white solid, which, on recrystallization from a large volume of absolute alcohol, gave the ketone (3c) (3.60 g, 88%) as needles, m.p. 233—234 °C (from EtOH) (lit.,[7] 231 °C), R_F 0.37 (EtOAc), $\nu_{max.}$ 1 695 (C=O), 1 440 (P–Ph), and 1 185 cm^{-1} (P=O); *m*/*z* 410 (M^+, 22%), 219 ($Ph_2PO_2H_2^+$, 68), and 201 (Ph_2PO^+, 100) (Found: M^+, 410.1450. $C_{27}H_{23}O_2P$ requires *M*, 410.1436).

The following compounds, (3a), (3b), and (3d)—(3f), were also prepared in a similar way by Method B.

1-*Diphenylphosphinoylpentan*-3-*one* (3b).—Ethyl vinyl ketone (0.41 g, 4.81 mmol) and diphenylphosphinous chloride (1.06 g, 4.81 mmol) gave, after chromatography on silica (eluted with EtOAc), the *ketone* (987 mg, 72%) (see above).

4-*Diphenylphosphinoylpentan*-2-*one* (3a). (*a*) Pent-3-en-2-one (1.76 g, 21.0 mmol) and diphenylphosphinous chloride (4.4 g, 20.0 mmol) gave, after chromatography on silica (eluted with EtOAc), the *ketone* (3.78 g, 66%) (see above).

(*b*) The same procedure but with acetonitrile as solvent gave the *ketone* (3a) (3.04 g, 53%).

3-*Diphenylphosphinoylcyclohexanone* (3d). Cyclohex-2-enone (1.06 g, 11 mmol) and diphenylphosphinous chloride (2.2 g, 10 mmol) gave, after chromatography on silica (eluted with EtOAc), the *ketone* (3d) (1.96 g, 66%) as needles, m.p. 154—155 °C (from EtOAc), R_F 0.14 (EtOAc); δ ($CDCl_3$) 1.70—2.94 (9 H, m, ring CH's), 7.36—7.94 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 715 (C=O), 1 440 (P–Ph), and 1 185 cm^{-1} (P=O); *m*/*z* 298 (M^+, 9%), 202 (Ph_2POH^+, 100), and 201 (Ph_2PO^+, 68) (Found: M^+, 298.1093. $C_{18}H_{19}O_2P$ requires *M*, 298.1122).

Methyl 3-*diphenylphosphinoylpropionate* (3e). Methyl acrylate (0.43 g, 5 mmol) and diphenylphosphinous chloride (1.06 g, 4.8 mmol) gave, on being stirred overnight at room temperature under nitrogen, the *ester* (3e) (703 mg, 51%) as needles, m.p. 73—74 °C (from EtOAc) (Found: C, 66.5; H, 5.95; P, 10.9. $C_{16}H_{17}O_3P$ requires C, 66.7; H, 5.95; P, 10.7%), R_F 0.20 (EtOAc); δ ($CDCl_3$) 2.40 (4 H, br s, PCH_2CH_2), 3.35 (3 H, s, OMe), and 7.10—7.70 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 745 (C=O), 1 435 (P–Ph), and 1 175 cm^{-1} P=O); *m*/*z* 288 (M^+, 1.3%), 273 (*M* − Me, 5), 257 (*M* − OMe, 17), 229 (*M* − CO_2Me, 5), and 201 (Ph_2PO^+, 100) (Found: M^+, 288.0928. $C_{16}H_{17}O_3P$ requires *M*, 288.0916).

Ethyl 3-*diphenylphosphinoylbutanoate* (3f). Ethyl crotonate (0.55 g, 4.8 mmol) and diphenylphosphinous chloride (1.06 g, 4.8 mmol) gave, after column chromatography on silica (eluted with EtOAc), the *ester* (3f) (878 mg, 56%) as an oil, R_F 0.09 (EtOAc); δ ($CDCl_3$) 1.14 (3 H, t, J_{HH} Hz, CH_2Me), 1.16 (3 H, dd, J_{HH} 7 Hz, J_{PH} 15 Hz, PCH*Me*), 2.20—2.84 (3 H, m, $PCHCH_2$), 4.05 (2 H, q, J_{HH} 7 Hz, CH_2Me), and 7.26—7.94 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 745 (CO_2Et), 1 435 P–Ph), and 1 180 cm^{-1} (P=O); *m*/*z* 316 (M^+, 1%), 244 ($Ph_2POCHMe_2^+$, 26), 202 (Ph_2POH^+, 100), and 201 (Ph_2PO^+, 46) (Found: M^+, 316.1248. $C_{18}H_{21}O_3P$ requires *M*, 316.1228).

3-*Diphenylphosphinoylcyclohexanone* (3d) *by Method C*.—Cyclohex-2-enone [27] (1.0 g) was added to a solution of diphenylphosphinoylmagnesium bromide prepared [4] from bromobenzene (4.71 g), magnesium turnings (0.8 g), and diethyl phosphite (1.4 g) in THF (10 ml). After 36 h, the solvent was removed under reduced pressure and HCl (3 ml) in water (10 ml) was added followed by water (20 ml). The aqueous layer was washed with dichloromethane (4 × 10 ml) and the combined organic layers were washed with 10% aqueous sodium carbonate (10 ml) and water (10 ml), and dried ($MgSO_4$). Evaporation of the solvent gave ketone (3d) (1.86 g, 62%).

Synthesis of Ketone (3a) *by Method D* (*Table* 2).—2-*Chloro*-4-*diphenylphosphinoylpent*-1-*ene* (17; R^1 = Me). Ethyldiphenylphosphine oxide (250 mg, 1.09 mmol) was stirred in dry THF (20 ml), at −78 °C and under nitrogen, with BuLi (0.77 ml, 1.20 mmol) for 0.25 g, to give a deep red solution of the lithium salt. The solution was warmed to −25 °C, copper(I) iodide (230 mg, 1.20 mmol) added, and the mixture stirred for 0.75 h, 2,3-Dichloropropene (0.133 g, 1.20 mmol) was

added dropwise, and the black ' solution ' stirred for 0.5 h at −25 °C; it was then allowed to warm to room temperature and stand overnight. Concentrated ammonia solution (*d* 880, 4 drops) and saturated aqueous ammonium chloride (30 ml) were then added and the deep blue solution extracted with CH_2Cl_2 (4 × 25 ml); 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 (eluted with EtOAc) gave 2-*chloro*-4-*diphenylphosphinoylpent*-1-*ene* (17; R^1 = Me) (226 mg, 68.3%) as needles, m.p. 122—124 °C (from EtOAc), R_F 0.23 (EtOAc), δ ($CDCl_3$) 1.14 (3 H, d, J_{HH} 7 Hz, J_{PH} 16 Hz, Me), 2.40—2.94 (3 H, m, PC*H*MeCH_2), 5.17 (2 H, br s, =CH_2), and 7.30—7.96 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 630 (C=C), 1 440 (P–Ph), and 1 180 cm^{-1} (P=O); *m/z* 304 (M^+, 1%), 269 (100, M − Cl), and 201 (68, Ph_2PO) (Found: M^+, 304.0754. $C_{17}H_{18}ClOP$ requires M, 304.0783).

Hydrolysis of the vinyl chloride (17; R^1 = Me) *to the ketone* (3a). The vinyl chloride (17; R^1 = Me) (100 mg, 0.33 mmol) dissolved in methanol (0.5 ml) was added to a vigorously stirred mixture of concentrated sulphuric acid (96%, 3 ml) and water (1 drop) kept at −5 °C. After 2 h the mixture was poured onto ice (100 g), and neutralised with 10% aqueous sodium carbonate. Extraction with chloroform (3 × 25 ml) drying of the combined organic layers (Na_2SO_4), and evaporation under reduced pressure gave an oil. P.l.c. on silica (eluted with EtOAc) then gave the ketone (3a) (72 mg, 77%).

3-*Diphenylphosphinoyl*-1-*phenylpropan*-1-*ol* (19; R^1 = H).—A solution of diphenylmethylphosphine oxide (2.16 g) in dry THF (50 ml) was stirred under nitrogen with n-butyl-lithium (7.4 ml, 15% in hexane) at room temperature for 0.5 h. Styrene oxide (1.2 g) was slowly added to the solution which then stirred for 4 h. Aqueous ammonium chloride solution (100 ml) was added. The resulting aqueous layer was separated and extracted with methylene chloride (3 × 50 ml). The combined organic layers were dried ($MgSO_4$) and the solvents removed by evaporation under reduced pressure to give a crude residue which crystallised on cooling to give the *alcohol* (3.25 g, 96%). The alcohol was purified by recrystallisation from ethyl acetate–di-isopropyl ether; it had m.p. 141—143 °C; R_F (EtOAc–MeOH, 9 : 1) 0.52; $\nu_{max.}$ 3 300 (OH), 1 439 (Ph–P), and 1 165 cm^{-1} (P=O); δ ($CDCl_3$) 7.1—7.8 (m, 15 H, ArH), 4.76 (1 H, br t, Ph–C*H*, J_{HH} 5 Hz), 4.65 (br s, 1 H, exch., OH), and 1.8—2.5 (4 H, m, PCH_2CH_2); *m/z* 336 (14%, M^+), 318 (13%, $M^+ - H_2O$), 230 (65%, M^+ − PhCHOH) 215 [79%, $M^+ - CH_2CH(Ph)OH$], 202 (100%, Ph_2POH^+), and 201 (80%, Ph_2PO^+).

3-*Diphenylphosphinoyl*-1-*phenylbutan*-1-*ol* (19; R^1 = Me).—To a solution of n-butyl-lithium (7.4 ml; 15% in hexane) in dry ether (100 ml) was added diphenyl(ethyl)phosphine oxide (2.3 g) in a dry nitrogen atmosphere at room temperature. After 30 min the reaction mixture was cooled to 5 °C and styrene oxide (1.3 ml) was injected slowly with a syringe. The reaction mixture was kept in an ice-bath for 1 h and then allowed to warm to room temperature. Aqueous ammonium chloride (50 ml) was added and the resulting solution stirred for 15 min. Methylene chloride (50 ml) was added and the aqueous layer separated. The aqueous layer was extracted with methylene chloride (3 × 20 ml). The combined organic layers were dried ($MgSO_4$) and the solvents removed by evaporation under reduced pressure to give a residual oil. This was taken up in boiling ether, and the *alcohol* (2.3 g, 65%) crystallised out on cooling. The alcohol could be purified by recrystallisation from ether; it had m.p. 167—169 °C; R_F (EtOAc) 0.17 and 0.23 for the two diastereoisomers; $\nu_{max.}$ 3 320 (OH), 1 442 (Ph–P), and 1 170 cm^{-1} (P–O); δ ($CDCl_3$) 7.1—7.9 (15 H, m, ArH), 4.78 (1 H, br t, Ph–C*H*OH, J_{HH} 6.5 Hz), 4.7 (1 H, br s, exch., OH), 3.0 (1 H, m, P–C*H*–Me for diastereoisomer), 2.5 (1 H, m, P–C*H*–Me for the other diastereoisomer), 2.0 (2 H, m, P–C–CH_2), 1.26 (3 H, dd, P–CH–*Me*, J_{PH} 7 Hz, J_{HH} 3 Hz, for one diastereoisomer), and 1.1 (3 H, dd, P–CH–*Me*, J_{PH} 7 Hz, J_{HH} 3 Hz, for the other diastereoisomer); *m/z* 350 (4.5%, M^+), 332 (2%, $M^+ - H_2O$), 224 (90%, M^+ − PhCHOH), 230 [90%, $M^+ - CH_2CH(Ph)OH$], 202 (90%, Ph_2POH^+), and 201 (100%, Ph_2PO^+ (Found: C, 75.1; H, 6.8; P, 8.85. $C_{22}H_{23}O_2P$ requires C, 75.19; H, 6.62; P, 8.84%).

3-*Diphenylphosphinoyl*-1-*phenylbutan*-1-*one* (3h) *by Method E.*—3-Diphenylphosphinoyl-1-phenylbutan-1-ol (19; R^1 = Me) (0.5 g) was stirred in solution in acetone (10 ml) and a solution of Jones's reagent [14] prepared from CrO_3 (26.7 g) and concentrated H_2SO_4 (23 ml) made up to 100 ml with water was added dropwise until an orange colouration just persisted in the green mixture (*ca.* 0.5 ml required). This solution was stirred for 30 min and then isopropyl alcohol was added. The mixture was stirred for 15 min, then water was added, the mixture extracted with chloroform, dried ($MgSO_4$), and evaporated. Column chromatography (EtOAc–5% MeOH) gave the *ketone* (3h) (304 mg, 61%) as a glass, R_F 0.2, δ ($CDCl_3$) 7.2—8.1 (15 H, m, Ph_2PO and Ph), 2.9—3.6 (3 H, m, PC*H*–CH_2), 1.23 (3 H, dd, J_{HH} 6 Hz and J_{PH} 15 Hz, PCMe). It was characterised as the ethylene acetal.[21]

3-*Diphenylphosphinoyl*-1-*phenylpropan*-1-*one* (3g).—In a similar way, 3-diphenylphosphinoyl-1-phenylpropan-1-ol (19; R^1 = H) (332 mg) and Jones's reagent [14] gave, after a work-up similar to the above using aqueous sodium hydrogen carbonate instead of water, the *ketone* (3g) (302 mg, 91%), R_F 0.3, δ ($CDCl_3$) 7.0—8.1 (15 H, m, Ph_2PO and Ph) and 2.3—3.7 (4 H, m, PCH_2CH_2). This ketone also was characterised as its ethylene acetal.[21]

Ketone (3g) *following the Procedure of Mueller and Di Pardo.*[28]—3-Diphenylphosphinoyl-1-phenylpropan-1-ol (2.7 g) was stirred in acetone (100 ml) and Jones's reagent [14] added slowly until the orange colouration persisted in the solution for 10 min without further addition. Isopropyl alcohol was added to reduce the excess of reagent. A solution of trisodium citrate (8 g) in water (30 ml) was added, followed by amalgamated zinc dust (90 mg). This solution was stirred for 10 min and then aqueous sodium hydroxide was added, giving a clear green solution; this was extracted with ether, dried ($MgSO_4$), and evaporated. The crude material was dissolved in chloroform, washed with water, dried ($MgSO_4$), and re-evaporated to give the ketone (3g) (2.6 g, 97%), pure by t.l.c. and n.m.r.

2-(*Diphenylphosphinoylmethyl*)*cyclohexanone* (3i) *by Method E.*—2-(*Diphenylphosphinoylcyclohexanol* (22; R^1 = H). BuLi (6.6 ml, 10.2 mmol) was added dropwise to a stirred solution of methyldiphenylphosphine oxide (2 g, 9.3 mmol) in dry THF (20 ml) under nitrogen at −78 °C. After 10 min, cyclohexene oxide (1.0 g, 10.2 mmol) was added dropwise at −78 °C after which the solution was heated under reflux for 12 h, under nitrogen. Aqueous NH_4Cl (20 ml) was added, the layers separated, and the aqueous layer extracted with EtOAc (3 × 20 ml); the combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give an orange oil; crystallisation of this from EtOAc–light petroleum (b.p. 60—80 °C) (1 : 1) gave the *alcohol* (22; R^1 = H) (2.22 g, 76%) as needles, m.p. 151—152 °C, R_F 0.29 (EtOAc), δ ($CDCl_3$) 0.70—2.30 (8 H, m, ring CH_2's) 2.50—3.15 (4 H, m, C*H*OH and PCH_2CH), 4.60 (1 H, s, OH), and 7.15—7.80 (10 H, m, Ph_2PO); $\nu_{max.}$ 3 350 (OH), 1 440 (P–Ph), and 1 155 cm^{-1} (P=O); *m/z* 314 (M^+, 6%), 215 ($Ph_2POCH_2^+$, 47), 202 (Ph_2-

POH$^+$, 100), and 201 (Ph_2PO^+, 24) (Found: M^+, 314.1451. $C_{19}H_{23}O_2P$ requires M, 314.1436).

Oxidation of 2-(*diphenylphosphinoylmethyl*)*cyclohexanol* (22; R^1 = H) *with pyridinium dichromate*. A solution of the alcohol (22; R′ = H) (314 mg, 1 mmol) in dry DMF (2 ml) was added dropwise with stirring to a suspension of pyridinium dichromate [15] (750 mg, 2.53 mmol) in dry DMF (2 ml) at room temperature and under nitrogen. Stirring was continued for 2 days after which the mixture was worked up by addition of sodium citrate (1 g) and ' mossy zinc ' [28] (10 mg) and stirred for 10 min at room temperature. Aqueous sodium hydroxide was added until the mixture was alkaline, after which it was extracted with dichloromethane (4 × 20 ml); the combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure gave an oil. P.l.c. of this on silica (eluted with EtOAc) gave 2-(*diphenylphosphinoylmethyl*)*cyclohexanone* (3i) (286 mg, 91%) as a colourless oil, R_F 0.19 (EtOAc), δ ($CDCl_3$) 1.30—2.50 (10 H, m, ring CH's and PCH_AH_B), 3.26 (1 H, ddd, *J* 4, 10, and 16 Hz, PCH_AH_B), and 7.30—7.88 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 710 (C=O), 1 435 (P–Ph), and 1 180 cm^{-1} (P=O); *m*/*z* 312 (M^+, 22%), 202 (Ph_2POH^+, 100), and 201 (Ph_2PO^+, 30) (Found: M^+, 312.1262. $C_{19}H_{21}O_2P$ requires M, 312.1245).

4-*Diphenylphosphinoyl*-3-*methylpentan*-2-*one* (3k) *by Method F*.—3-*Methoxybut*-1-*yne* (24; R^3 = Me). But-3-yn-2-ol (30 ml) was cooled to −10 °C and 12M-aqueous sodium hydroxide (30 ml) was added; the mixture was stirred for 10 min and then dimethyl sulphate (32 ml) added slowly. The solution was then allowed to warm to room temperature and then heated at 60 °C for 1 h. 3-Methoxybut-1-yne was distilled out of the reaction mixture (21 ml, 60%), b.p. 62—68 °C (lit.,[9] 64—68 °C), $\nu_{max.}$ 2 820 (OMe) and 2 100 cm^{-1} (C≡C); δ ($CDCl_3$) 4.1 (1 H, dq, *J* 7, *J* 2 Hz, C*H*OMe), 3.4 (3 H, s, OMe), 2.5 (1 H, d, *J* 2 Hz, CH≡C), and 1.4 (3 H, d, *J* 7 Hz, CH*Me*).

3-*Methoxybutan*-2-*one* (25; R^3 = Me). 3-Methoxybut-1-yne (9.6 g) was stirred at room temperature in glacial acetic acid (100 ml) and (10 ml) of a solution of mercuric oxide (4 g), sulphuric acid (10 ml, 98%), and water (100 ml) was added drop by drop, followed by a few drops of acetic acid to ensure complete mixing. The solution was kept at 40 °C for 4.5 h and then neutralised with aqueous sodium hydroxide and extracted with ether. The ether extracts were dried (anhydrous potassium carbonate) and evaporated under reduced pressure to remove the ether; the remaining pale lemon oil was distilled to give the methoxy ketone (6.5 g, 60%), b.p. 110—113 °C, $\nu_{max.}$ 2 820 (OMe) and 1 715 cm^{-1} (C=O); δ ($CDCl_3$) 3.65 (1 H, q, *J* 7 Hz, C*H*OMe), 3.3 (3 H, s, OMe), 2.1 (3 H, s, CMe), and 1.25 (3 H, d, *J* 7 Hz, CHMe).

2-*Diphenylphosphinoyl*-4-*methoxy*-3-*methylpentan*-3-*ol* (26; R^1 = R^3 = Me). The procedure used was the same as that previously described.[3] Ethyldiphenylphosphine oxide (1.5 g) in dry ether (50 ml), n-butyl-lithium (3 ml; 2M in hexane) for 0.5 h, and 3-methoxybutan-2-one (750 mg) in dry ether (25 ml) gave a white solid containing both diastereoisomers of the alcohol (26; R^1 = R^3 = H) which were separated by fractional recrystallisation from ethyl acetate. First crystallised *isomer* (1 g, 45%), m.p. 181—182 °C (from EtOAc), R_F 0.7, $\nu_{max.}$ 3 320 (OH), 1 435 (PPh), and 1 170 cm^{-1} (P=O); δ ($CDCl_3$) 7.4—8.05 (10 H, m, Ph_2PO), 4.1 (1 H, br m, OH), 3.55 (1 H, q, J_{HH} 6 Hz, MeOC*H*Me), 2.9—3.2 (1 H, quint, J_{PH} = J_{HH} = 8 Hz, PC*H*Me), 2.6 (3 H, s, OMe), 1.2 [3 H, s, C(OH)*Me*], 1.15 (3 H, d, J_{HH} 6 Hz, MeOCH*Me*), and 1.15 (3 H, dd, J_{PH} 18, J_{HH} 7 Hz, PCH*Me*); *m*/*z* 332 (17$^+$, 15%), 273 (*M* − MeCHOMe, 100), 230 (Ph_2POEt, 20), and 201 (Ph_2PO, 40) (Found: C, 68.5; H, 7.4; P, 9.0. $C_{19}H_{25}O_3P$ requires C, 68.7; H, 7.5; P, 9.3%); and the second recrystallised *isomer* (650 mg, 30%), m.p. 173—175° (from EtOAc–di-isopropyl ether), R_F 0.7, $\nu_{max.}$ 3 320 (OH), 1 435 (PPh), and 1 160 cm^{-1} (P=O); δ ($CDCl_3$) 7.4—8.1 (10 H, m, Ph_2PO), 4.7 (1 H, br s, OH), 3.55 (1 H, q, J_{HH} 6 Hz, MeC*H*OMe), 3.1 (3 H, s, OMe), 2.95 (1 H, m, PC*H*Me), 1.2 (3 H, s, *Me*COH), 1.2 (3 H, dd, J_{PH} 18, J_{HH} 7 Hz, PCH*Me*), and 1.15 (3 H, d, J_{HH} 6 Hz, *Me*CHOMe); *m*/*z* 332 (M^+, 5%), 273 (100), 230 (Ph_2POEt, 20), and 201 (Ph_2PO, 15) (Found: C, 68.7; H, 7.6; P, 9.0. $C_{19}H_{23}O_3P$ requires C, 68.7; H, 7.5; P, 9.3%).

Trifluoroacetolysis of the methoxy alcohol (26; R^1 = R^2 = Me). The alcohol (100 mg) was kept at room temperature in trifluoroacetic acid (0.4 ml) for 24 h. The solution was then poured onto anhydrous potassium carbonate and extracted with chloroform (50 ml). The chloroform extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give 4-*diphenylphosphinoyl*-3-*methylpentan*-2-*one* (3k) (70 mg, 80%), m.p. 102—103 °C (from di-isopropyl ether), R_F 0.6, $\nu_{max.}$ 1 705 (C=O), 1 440 (PPh), and 1 170 cm^{-1} (P=O); δ ($CDCl_3$) 7.4—8.0 (10 H, m, Ph_2PO), 3.2 (1 H, d quint, J_{PH} = J_{HH} = 7 Hz, J_{HH} 3 Hz, PC*H*Me), 2.95 (1 H, m, PCC*H*Me), 2.05 (3 H, s, COMe), 1.3 (3 H, d, J_{HH} 7 Hz, PCCH*Me*), and 1.15 (3 H, dd, J_{PH} 17, J_{HH} 7 Hz, PCH*Me*); *m*/*z* 300 (M^+, 2%), 299 (*M* − H, 2), 257 (*M* − $COCH_3$, 20), 244 (40), 230 (Ph_2POEt, 20), and 201 (Ph_2PO, 100) (Found: C, 71.7; H, 7.1; P, 10.1. $C_{18}H_{21}O_2P$ requires C, 72.0; H, 7.0; P, 10.3%).

4-*Diphenylphosphinoyl*-2-*methoxy*-3-*methylhexan*-3-*ol* (26; R^1 = Et, R^3 = Me).—Butyl-lithium (6.8 ml; 1.5M in hexane) was added to a solution of propyldiphenylphosphine oxide (2 g) in dry THF (30 ml) at 0 °C under nitrogen. After 10 min 3-methoxybutan-2-one (neat) was added dropwise until the red colour of the solution was discharged. Saturated aqueous ammonium chloride was added and the mixture extracted with ether; the organic solution was dried ($MgSO_4$) and evaporated. The resulting gum was separated by column chromatography (EtOAc) into a mixture of two diastereoisomers of the *alcohol* (1.5 g, 52%), m.p. 103—130 °C (from EtOAc), R_F 0.5, δ ($CDCl_3$) 0.88 and 0.79 (3 H, two t, J_{HH} 7 Hz, CH*Me*), 1.05—1.3 (6 H, m, OCMe and OCH*Me*), 1.5—2.1 (2 H, m, PCHCH_2Me), 2.65—2.9 (1 H, m, PC*H*CH_2), 2.41 and 3.19 (3 H, two s, OMe), 3.3—3.7 (1 H, m, J_{HH} 6 Hz and other splittings; OC*H*Me), 5.0 (1 H, br, OH), and 7.3—8.1 (10 H, m, Ph_2PO); *m*/*z* 347 (*M* + H, 2%), 287 (*M* − C_3H_7O, 100), 244 (11), 299 (33), 219 (13), and 201 (Ph_2PO^+, 77) (Found: *M* − OMe, 315.1488. $C_{19}H_{24}O_2P$ requires M, 315.1513), together with further gummy products (1.2 g), possibly the other diastereoisomers of the alcohol (26; R^1 = Et, R^3 = Me) which could not be characterised.

4-*Diphenylphosphinoyl*-3-*methylhexan*-2-*one* (31) *by Method F*.—Alcohol (26; R^1 = Et, R^2 = Me) (512 mg) and TFA were stirred together at room temperature for 24 h and then poured into a stirred slurry of potassium carbonate in chloroform. The solids were filtered off and the organic solution dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography giving an approximately 3 : 5 (by n.m.r.) mixture of diastereoisomers of the *ketone* (31) (275 mg, 59%), a yellow gum R_F 0.3, δ ($CDCl_3$) 0.80 (minor) and 1.33 (major) (3 H, two t, each J_{HH} 7 Hz, CH_2Me), 1.13 (minor) and 1.33 (major) (3 H, two d, each J_{HH} 7 Hz, CH*Me*), 1.5—1.9 (2 H, m, PCHCH_2Me), 2.02 (major) and 2.14 (minor) (3 H, two s, COMe), 2.6—3.4 (2 H, m, PCH and COCH), 7.2—8.0 (10 H, m, Ph_2PO); *m*/*z* 314 (M^+, 0.4%), 286 (2), 244 (11), and 201 (Ph_2PO^+, 100) (Found: M^+, 314.1439. $C_{19}H_{23}O_2P$ requires M, 314.1435).

1-*Diphenylphosphinoyl*-3-*methoxy*-2-*methylbutan*-2-*ol* (26; R^1 = H, R^3 = Me).—Methyldiphenylphosphine oxide (4 g)

was stirred in solution in dry THF (60 ml) at 0 °C under a stream of dry nitrogen. n-Butyl-lithium (13.6 ml; 1.5M-solution in hexane) was added dropwise and the mixture stirred for 10 min. 3-Methoxybutan-2-one was added dropwise until the anion colour was discharged and the solution then stirred for a further 10 min. Saturated aqueous ammonium chloride solution (50 ml) was added, the mixture extracted with ether (3 × 50 ml), and the organic extracts combined, dried ($MgSO_4$), and evaporated to give a yellow gum. Column chromatography (EtOAc) gave the *HR_F isomer* of the *alcohol* (26; R^1 = H, R^3 = Me) (3.2 g, 54%), m.p. 95—97 °C, R_F 0.37, δ ($CDCl_3$) 1.11 (3 H, d, *J* 6 Hz, CH*Me*), 1.19 (3 H, d, J_{PH} 1 Hz, CMe), 2.54 (1 H, dd, J_{AB} 15 and J_{HP} 11 Hz, PCH), 2.87 (3 H, s, OMe), 2.94 (1 H, dd, J_{AB} 15, J_{HP} 9 Hz, PCH), 3.31 (1 H, q, *J* 6 Hz, C*H*Me), 4.7 (1 H, br, OH), and 7.3—8.0 (10 H, m, Ph_2PO); *m/z* 319 (*M* + H, 3%), 285 (7), 259 (92), 215 (62), and 201 (Ph_2PO^+, 100) (Found: C, 67.7; H, 7.3; P, 9.7. $C_{18}H_{23}O_3P$ requires C, 67.9; H, 7.3; P, 9.7%) and the *LR_F isomer* of the *alcohol* (1 g, 17%), m.p. 97—100 °C, R_F 0.3, δ ($CDCl_3$) 1.14 (3 H, d, *J* 7 Hz, CH*Me*), 1.26 (3 H, s, CMe), 2.63 (2 H, d, J_{PH} 10 Hz, PCH_2), 3.25 (3 H, s, OMe), 3.31 (1 H, q, *J* 7 Hz, C*H*Me), 4.1—4.7 (1 H, br, OH), and 7.3—8.0 (10 H, m, Ph_2PO); *m/z* 319 (*M* + H, 1%), 285 (8), 259 (*M* − C_3H_7O, 100), 239 (13), 215 (26), and 201 (Ph_2PO^+, 76) (Found: *M* + H, 319.1450. $C_{18}H_{24}O_3P$ requires *M*, 319.1463) and a mixture of the two isomers (1 g, 17%).

1-*Diphenylphosphinoyl*-2-*methylbutan*-3-*one* (3j) *by Method F*.—The *LR_F* isomer of the alcohol (26; R^1 = H, R^3 = Me) (315 mg) was heated with TsOH (200 mg) in dry toluene under reflux for 46 h. The mixture was cooled, poured into ether (100 ml), washed with aqueous sodium hydrogen carbonate (3 × 25 ml), dried ($MgSO_4$), and evaporated to give a brown gum. Preparative t.l.c. (ethyl acetate) gave the *ketone* (3j) (195 mg, 60%), m.p. 104—106 °C, R_F 0.15, $\nu_{max.}$ ($CHCl_3$) 1 710 (C=O), 1 438 (Ph–P), and 1 173 cm^{-1} (P=O); δ ($CDCl_3$) 1.22 (3 H, d, *J* 7 Hz, CH*Me*), 2.04 (3 H, s, COMe), 2.0—2.2 (1 H, m, C*H*Me), 2.8—3.3 (2 H, m, PCH_2), and 7.3—7.9 (10 H, m, Ph_2PO); *m/z* 286 (M^+, 7%), 271 (3), 244 (58), and 202 (Ph_2POH^+, 100) (Found: C, 71.2; H, 6.6; P, 10.6. $C_{17}H_{19}O_2P$ requires C, 71.3; H, 6.7; P, 10.8%).

1-*Diphenylphosphinoyl*-3-*methoxy*-2-*methylpropan*-2-*ol*.—In a similar way, methyldiphenylphosphine oxide (1 g), n-butyl-lithium (3.4 ml; 1.5M in hexane) and methoxyacetone in dry THF (20 ml) at −78 °C gave, after the usual work-up procedure followed by recrystallization from ethyl acetate, the *alcohol* (1.25 g, 89%), m.p. 112—115 °C, R_F 0.25, δ ($CDCl_3$) 7.4—7.9 (10 H, m, Ph_2PO), 3.28 (1 H, d, J_{AB} 9 Hz, CH_2*O-Me), 3.15 (1 H, d, J_{AB} 9 Hz, CH_2*OMe), 2.96 (3 H, s, OMe), 2.81 (1 H, dd, J_{AB} 15 Hz, and J_{PH} 10 Hz, PCH_2*), 2.51 (1 H, dd, J_{AB} 15 Hz and J_{PH} 11 Hz, PCH_2*), and 1.28 (3 H, d, J_{PH} 2 Hz, CMe); *m/z* 305 (*M* + H, 2%), 286 (18), 271 (20), 259 (*M* − C_2H_5O, 100), 215 (28), and 201 (Ph_2PO^+, 77) (Found: C, 66.8; H, 7.0; P, 10.0. $C_{17}H_{21}O_3P$ requires C, 67.1; H, 7.0; P, 10.2%).

2-*Diphenylphosphinoyl*-3,5-*dimethylhex*-3-*ene* (31; R^1 = R^2 = Me, R^3 = Pr^i).—By the method previously reported,[3,9] diphenylethylphosphine oxide (5 g), BuLi (10 ml; 2M in hexane) and 4-methylpentan-2-one (2.5 g) in dry ether (50 ml) gave tertiary alcohol (30; R^1 = R^2 = Me, R^3 = Pr^i) which was dehydrated with TFA (20 ml) to give the *phosphine oxide* (31; R^1 = R^2 = Me, R^3 = Pr^i), as a single geometrical isomer, (5 g, 80%), m.p. 159—160 °C, R_F 0.5, $\nu_{max.}$ 1 440 (PPh) and 1 170 cm^{-1} (P=O); δ ($CDCl_3$) 0.6 and 0.85 (6 H, two d, *J* 7 Hz, $CHMe_2$*), 1.35 (3 H, dd, J_{PH} 16, J_{HH} 7 Hz, PCH*Me*), 1.7 (3 H, br s, MeC=C), 2.35 (1 H, m, Me_2CH), 3.05 (1 H, quintet, J_{PH} = J_{HH} 7 Hz, PC*H*Me), 1.7 (3 H, br s, MeC=C), 2.35 (1 H, m, Me_2CH), 3.05 (1 H, quintet, J_{PH} = J_{HH} 7 Hz, P C*H*Me), 5.0 (1 H, br dd, *J* 9, 4 Hz, C=CH), and 7.35—8.00 (10 H, m, Ph_2PO); *m/z* 312 (M^+, 10%), 302 (10), 269 (*M* − C_3H_7, 20), and 201 (Ph_2PO, 100) (Found: C, 76.8; H, 8.1; P, 9.8. $C_{20}H_{26}OP$ requires C, 76.9; H, 8.0; P, 9.9%).

1-*Diphenylphosphinoyl*-2,4-*dimethylpent*-2-*ene* (31; R^1 = H, R^2 = Me, R^3 = Pr^i).—In the same way, methyldiphenylphosphine oxide (1 g), 4-methylpentan-2-one (0.5 g) and BuLi (3 ml) in THF (25 ml) gave the alcohol (30; R^1 = H, R^2 = Me, R^3 = Pr^i) (1.17 g, 80%), m.p. 90—92 °C, δ ($CDCl_3$) 0.85 and 0.95 (each 3 H, d, *J* 7 Hz, $CHMe)_2$* 1.28 (3 H, s, CMe), 1.5 (2 H, m, CH_2), 1.8 (1 H, m, C*H*Me_2), 2.4—2.8 (2 H, ABP system, J_{AP} 10, J_{BP} 11, J_{AB} 15 Hz, PCH_2), 4.55 (1 H, s, OH), and 7.4—7.9 (10 H, m, Ph_2PO). Dehydration of this alcohol (0.75 g) in TFA (10 ml) at 70 °C for 30 min gave the *allyl phosphine oxide* (31; R^1 = H, R^2 = Me, R^3 = Pr^i) (0.7 g, 94%) (containing a trace of the *Z*-isomer), δ ($CDCl_3$) (0.78 (6 H, d, *J* 7 Hz, $CHMe_2$), 1.78 (3 H, narrow m, C=CMe), 2.4 (1 H, m, C*H*Me_2), 3.06 (2 H, d, J_{PH} 13 Hz, PCH_2), 4.82 (1 H, m, C=CH), and 7.4—7.9 (10 H, m, Ph_2PO), converted directly into the epoxide (38; R^1 = H, R^2 = Me, R^3 = Pr^i).

1-(*Diphenylphosphinoylmethyl*)*cyclopentanol* [30; R^1 = H, R^2R^3 = $(CH_2)_3$].—BuLi (1.5 ml, 2.2 mmol) was added dropwise to a stirred solution of methyldiphenylphosphine oxide (432 mg, 2 mmol) in dry THF (20 ml), under nitrogen at −78 °C. After 10 min, cyclopentanone (185 mg, 2.2 mmol) was added dropwise at −78 °C, the solution allowed to warm to room temperature, and aqueous NH_4Cl (20 ml) added. The layers were separated, the aqueous layer extracted with EtOAc (3 × 25 ml), and the combined organic layers dried (Na_2SO_4) and evaporated under reduced pressure to give a white solid. Recrystallisation from EtOAc gave the *alcohol* (420 mg, 70%) as needles, m.p. 121—122 °C (from EtOAc) (Found: C, 71.8; H, 7.20; P, 10.3. $C_{18}H_{21}O_2P$ requires C, 72.0; H, 7.05; P, 10.3%), R_F 0.36 (EtOAc), δ ($CDCl_3$) 1.20—1.90 (8 H, m, ring CH_2's), 3.73 (2 H, d, J_{PH} 10 Hz, PCH_2), 4.90 (1 H, br s, OH), and 7.30—7.90 (10 H, m, Ph_2PO); $\nu_{max.}$ 3 300 (OH), 1 440 (P–Ph), and 1 170 cm^{-1} (P=O); *m/z* (M^+ absent), 282 (*M* − H_2O, 24%), 215 ($Ph_2POCH_2^+$, 100), 202 (Ph_2POH^+, 22), and 201 (Ph_2PO^+, 24) (Found: M^+ − H_2O, 282.1195. $C_{18}H_{19}OP$ requires *M*, 282.1174).

1-(*Diphenylphosphinoylmethyl*)*cyclopentene* [31; R^1 = H, R^2R^3 = $(CH_2)_3$].—The above alcohol (142 mg, 0.47 mmol) was heated under reflux with an excess of TFA (5 ml) for 2 min, after which the solution was poured onto ice and extracted with chloroform (3 × 25 ml). The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate solution (3 × 50 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give an off-white solid. Recrystallisation of this from EtOAc gave the *allyl phosphine oxide* (118 mg, 89%) as needles, m.p. 140—141 °C (from EtOAc) (Found: C, 76.5; H, 7.00; P, 11.0. $C_{18}H_{19}OP$ requires C, 76.6; H, 6.80; P, 11.0%), R_F 0.39 (EtOAc), δ ($CDCl_3$) 1.76 (2 H, quint, J_{HH} 8 Hz, $CH_2CH_2CH_2$), 2.24 (4 H, br t, J_{HH} 9 Hz, $CH_2CH_2CH_2$), 3.18 (2 H, br d, J_{PH} 15 Hz, PCH_2), 5.44 (1 H, m, =CH), and 7.30—7.90 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 440 (P–Ph) and 1 185 cm^{-1} (P=O); *m/z* 282 (M^+, 62%) and 201 (Ph_2PO^+, 100) (Found: M^+, 282.1198. $C_{18}H_{19}OP$ requires *M*, 282.1173).

1-(*Diphenylphosphinoylmethyl*)*cycloheptanol* [30; R^1 = H, R^2R^3 = $(CH_2)_5$].—BuLi (6.6 ml, 10.2 mmol) was added dropwise to a stirred solution of methyldiphenylphosphine oxide (2 g, 9.3 mmol) in dry THF (20 ml) under nitrogen at

−78 °C. After 10 min cycloheptanone (1.16 g, 10.2 mmol) was added dropwise at −78 °C, the solution allowed to warm to room temperature, and aqueous NH_4Cl (25 ml) added. The layers were separated and the aqueous layer extracted with EtOAc (3 × 25 ml); the combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give a white solid. Recrystallisation of this from EtOAc gave the *alcohol* (2.71 g, 89%) as needles, m.p. 140—142 °C, R_F 0.40 (EtOAc), δ ($CDCl_3$) 1.10—2.10 (12 H, m, ring CH_2's), 2.62 (2 H, d, J_{PH} 10 Hz, PCH_2), 5.76 (1 H, s, OH), and 7.30—7.84 (10 H, m, Ph_2PO); $\nu_{max.}$ 3 340 (OH), 1 440 (P–Ph), and 1 165 cm^{-1} (P=O); *m/z* 328 (M^+, 12%), 310 ($M - H_2O$, 32), 215 ($Ph_2POCH_2^+$, 100), and 201 (Ph_2PO^+, 78) (Found: C, 73.2; H, 7.70; P, 9.6. $C_{20}H_{25}O_2P$ requires C, 73.2; H, 7.70; P, 9.4%).

1-(*Diphenylphosphinoylmethyl*)*cycloheptene* [31; R^1 = H, R^2R^3 = $(CH_2)_5$].—The above alcohol (2.5 g, 7.6 mmol) was heated under reflux with an excess of TFA (15 ml) for 1 h, after which the solution was cooled, poured into water (100 ml), and extracted with chloroform (3 × 25 ml). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (3 × 50 ml) and water (1 × 50 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give an oil, which slowly solidified. Recrystallisation of this from EtOAc–petroleum gave the *allyl phosphine oxide* (1.65 g, 70%) as needles, m.p. 102—104 °C (Found: C, 77.4; H, 7.60; P, 10.2. $C_{20}H_{23}OP$ requires C, 77.4; H, 7.50; P, 10.0%), R_F 0.36 (EtOAc), δ ($CDCl_3$) 1.20—2.28 (10 H, m, ring CH_2's), 3.08 (2 H, d, J_{PH} 16 Hz, PCH_2), 5.50 (1 H, dt, J_{HH} 5 and 6 Hz, =CH), and 7.30—7.86 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 440 (P–Ph) and 1 190 cm^{-1} (P=O); *m/z* 310 (M^+, 50%), and 201 (Ph_2PO^+, 100) (Found: M^+, 310.1494. $C_{20}H_{23}OP$ requires *M*, 310.1487).

Direct Conversion of Allyl Phosphine Oxides (31) *into Ketones* (3).—*Attempted hydroxylation of allyl phosphine oxide* (31; R^1 = R^2 = Me, R^3 = Pr^i) by *alkaline potassium permanganate*.[29] A solution of potassium permanganate (0.78 g) and sodium hydroxide (0.17 g) in water (27 ml) at 0 °C was added quickly with vigorous stirring to a cold (−5 °C) solution of the allyl phosphine oxide (1 g) in a mixture of t-butyl alcohol (33 ml), water (7 ml), and ice (17 g). After *ca.* 10 min most of the permanganate colour had been discharged. Sulphur dioxide was bubbled through the solution to reduce any excess of permanganate and traces of manganese dioxide were removed by filtration. The solution was evaporated to remove the t-butyl alcohol, the aqueous residue extracted with ether (4 × 30 ml), and the extracts dried and evaporated to give a cloudy colourless gum. This was dissolved in ethyl acetate, filtered through Hyflo, and crystallised, to give unchanged starting material by n.m.r. and t.l.c.

Attempted Preparation of the Ketone (34; R^1 = H) *from the Allyl Phosphine Oxide* (33; R^1 = H).—(a) *With iodine and silver acetate*. The allyl phosphine oxide (33; R^1 = H) (286 mg, 1 mmol) was heated under reflux in glacial acetic acid (5 ml) with silver acetate (170 mg, 1 mmol) and iodine (260 mg, 1 mmol) for 14 days. The solution was cooled, poured into dilute hydrochloric acid (50 ml), and extracted with chloroform (3 × 25 ml). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give an oil. P.l.c. on silica (eluted with EtOAc), gave recovered starting material (129 mg, 45%), together with the ketone (33; R^1 = H) (103 mg, 30%).

(b) *By hydroboration*. A solution of the allyl phosphine oxide (33; R^1 = H) (500 mg, 1.69 mmol) and boron trifluoride–ether complex (0.32 ml, 2.54 mmol) in dry THF (10 ml) was added slowly to a suspension of sodium borohydride (120 mg, 3.15 mmol) in dry THF (10 ml) under nitrogen and at room temperature, during 1 h, with stirring. The mixture was stirred a further 24 h at room temperature and then quenched with hydrogen peroxide (100 vol; 5 ml) and 10% aqueous sodium hydroxide (10 ml). Separation and extraction of the aqueous layer with EtOAc (4 × 20 ml), followed by washing of the combined organic layers with water (2 × 25 ml), drying (Na_2SO_4), and evaporation under reduced pressure gave a pale yellow oil. Column chromatography on silica (eluted with EtOAc), gave 1-(diphenylphosphinoylmethyl)cyclohexanol [22] (35) (82 mg, 15%) together with 2-(*diphenylphosphinoylmethyl*)-*cyclohexanol* (36) (307 mg, 58%) (see above). The recycling of (35) to (33; R^1 = H) has been described,[22] and the conversion of (36) into (33; R^1 = H) is described above.

Epoxides (38) *from Allyl Phosphine Oxides* (31) (*Table* 3).—2-*Diphenylphosphinoyl*-3,4-*epoxy*-3,5-*dimethylhexane* (38n). 2-Diphenylphosphinoyl-3,5-dimethylhex-3-ene (31; R^1 = R^2 = Me, R^3 = Pr^i) (500 mg) was dissolved in dry dichloromethane and stirred with sodium carbonate (170 mg). The solution was cooled to 0 °C and *m*-chloroperoxybenzoic acid (MCPBA) (360 mg of 85% reagent) added. The mixture was stirred for 20 h at room temperature. Dichloromethane (25 ml) was added to the resulting thick slurry which was filtered through Hyflo. The filtrate was washed with aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated under reduced pressure to give the *epoxide* (38n) (452 mg, 86%) as fine needles, m.p. 205—207 °C (from EtOAc), R_F 0.37, δ ($CDCl_3$) 7.4—8.1 (10 H, m, Ph_2PO), 2.4 (1 H, d, *J* 9 Hz, OCH), 2.3 (1 H, quint., J_{PH} 16 Hz and J_{HH} 7 Hz, PC*H*Me), 1.5 (3 H, s, OCMe), 1.45 (3 H, dd, J_{PH} 16, J_{HH} 7 Hz, PCH*Me*), 1.0—1.5 (1 H, m, C*H*Me_2), 0.97 (3 H, d, *J* 6 Hz, CHMe_2*), and 0.23 (3 H, d, *J* 6 Hz, CHMe_2*); *m/z* 328 (M^+, 2%), 313 (9), 285 (72), 256 (66), and 201 (Ph_2PO^+, 100) (Found: C, 73.2; H, 7.8; P, 9.5. $C_{10}H_{25}O_2P$ requires C, 73.2; H, 7.7; P, 9.4%).

1-*Diphenylphosphinoyl*-2,3-*epoxy*-2,4-*dimethylpentane* (38 m). Similarly, 1-diphenylphosphinoyl-2,4-dimethylpent-2-ene (31; R^1 = H, R^2 = Me, R^3 = Pr^i) (1.67 g), sodium carbonate (0.6 g), and MCPBA (1.26 g) in dichloromethane gave the *epoxide* (38m) (1.7 g, 97%) as fine needles, m.p. 133—135 °C (from EtOAc), R_F 0.35, ($CDCl_3$) 7.4—8.0 (10 H, m, Ph_2PO), 2.97 (1 H, dd, J_{PH} 12 Hz and J_{HH} 14 Hz, PCH_2*), 2.37 (1 H, d, *J* 10 Hz, OCH), 2.30 (1 H, dd, J_{PH} 11 Hz and J_{HH} 14 Hz, PCH_2*), 1.42 (3 H, s, OCMe), 1.1—1.8 (1 H, m, C*H*Me_2), 0.94 (3 H, d, *J* 7 Hz, CHMe_2*), and 0.94 (3 H, d, *J* 7 Hz, CHMe_2*); *m/z* 314 (M^+, 2%), 298 (5), 271 (18), 242 (26), 202 (Ph_2POH^+, 100), and 201 (Ph_2PO^+, 54) (Found: C, 72.6; H, 7.4; P, 9.6. $C_{19}H_{23}O_2P$ requires C, 72.6; H, 7.4; P, 9.9%).

1-*Diphenylphosphinoylmethyl*-6-*oxabicyclo*[3.1.0]*hexane* (38q). The allyl phosphine oxide [31; R^1 = H, R^2R^3 = $(CH_2)_3$] (500 mg, 1.74 mmol) was stirred with MCPBA (0.392 g, 1.93 mmol) and sodium carbonate (0.2 g, 1.93 mmol) in dichloromethane (25 ml), under nitrogen and at room temperature for 3 days. The sodium *m*-chlorobenzoate was filtered off through Hyflo, and the solvent evaporated under reduced pressure to give a white solid. Recrystallization from EtOAc gave the *epoxide* (38q) (485 mg, 92%) as a waxy solid, m.p. 92—94 °C (from EtOAc), R_F 0.35 (EtOAc), δ ($CDCl_3$) 1.20—2.00 (6 H, m, ring CH_2's), 2.64 (1 H, dd, $J_{H_AH_B}$ 12 Hz, J_{PH_A} 16 Hz, PCH_AH_B), 2.96 (1 H, dd, $J_{H_AH_B}$ 12 Hz, J_{PH_B} 14 Hz, PCH_AH_B), 3.18 (1 H, s, OCH), and 7.30—7.86 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 440 (P–Ph) and 1 185 cm^{-1} (P=O); *m/z* 298 (M^+, 4%), 215 ($Ph_2POCH_2^+$, 15), and 201 (Ph_2PO^+, 100) (Found: M^+, 298.1109. $C_{18}H_{19}O_2P$ requires *M*, 298.1122).

1-*Diphenylphosphinoylmethyl*-8-*oxabicyclo*[5.3.1]*octane* (38r). The allyl phosphine oxide [31; R^1 = H, R^2R^3 = $(CH_2)_5$] (500 mg, 1.6 mmol) was stirred with MCPBA (0.37 g, 1.8 mmol) and sodium carbonate (0.19 g, 1.8 mmol), under

nitrogen and at room temperature, for 3 days. The suspension was filtered through Hyflo, and the solvent evaporated under reduced pressure to give a white solid. Recrystallization of this from EtOAc gave the *epoxide* (38r) (510 mg, 97%) as needles, m.p. 136—137 °C (Found: C, 73.7; H, 7.25; P, 9.6. $C_{20}H_{23}O_2P$ requires C, 73.6; H, 7.10; P, 9.5%), R_F 0.32 (EtOAc), δ $CDCl_3$) 1.20—2.20 (10 H, m, ring CH_2's), 2.46 (1 H, dd, $J_{H_AH_B}$ 12 Hz, J_{PH_B} 14 Hz, PCH_AH_B), 2.94 (1 H, dd, J_{HH} *ca.* 3 and 4 Hz, OCH), and 7.34—7.96 (10 H, m, Ph_2PO); $\nu_{max.}$ 1 440 (P–Ph) and 1 185 cm^{-1} (P=O); *m/z* 326 (M^+, 2.6%) and 201 (Ph_2PO^+, 100) (Found: M^+, 326.1405. $C_{20}H_{23}O_2P$ requires *M*, 326.1435).

Epoxides (38) *without Isolation of the Allyl Phosphine Oxides* (31).—1-*Diphenylphosphinoyl*-2-*methyl*-2,3-*epoxybutane* (38j). Methyldiphenylphosphine oxide (2 g) in dry THF (30 ml) under dry nitrogen was stirred with n-butyllithium (6,8 ml of a 1.5M solution in hexane) at 0 °C for 10 min. Butan-2-one (1 ml) in dry THF (5 ml) was added and the mixture stirred for 5 min. Saturated aqueous ammonium chloride (30 ml) and ether (30 ml) were added. The aqueous layer was extracted with ether (3 × 30 ml) and the extracts dried ($MgSO_4$) and evaporated under reduced pressure to give the alcohol, R_F (EtOAc) 0.33. This was refluxed in TFA (20 ml) for 1 h and then poured into water (100 ml) and extracted with chloroform (4 × 30 ml); the extracts were washed with aqueous sodium hydrogen carbonate (3 × 30 ml), dried ($MgSO_4$), and evaporated to give the olefin (31; R^1 = H, R^2 = R^3 = Me). This crude material was dissolved in dry dichloromethane (60 ml) and stirred with sodium carbonate (1.1 g) and MCPBA (2.23 g) at room temperature for 4 days. The resulting slurry was filtered through Hyflo and the residue washed with dichloromethane. Evaporation gave a brown gum which was purified by column chromatography (EtOAc) to give the *epoxide* (38j) (1.7 g, 64% overall) as a mixture of diastereoisomers (*ca.* 2 : 1 by n.m.r.), m.p. 75—84 °C (from EtOAc), R_F 0.2, δ ($CDCl_3$), δ 7.3—8.0 (10 H, m, Ph_2PO), 2.94 (1 H, dd, J_{PH} 12 Hz and J_{AB} 14 Hz, PCH_2*), 2.7 (1 H, q, *J* 5 Hz, C*H*Me), 2.27 (1 H, dd, J_{PH} 12 Hz and J_{AB} 14 Hz, PCH_2*), 2.4—3.0 (signals for PCH_2 and C*H*Me from minor isomer), 1.38 (3 H, s, CMe), and 1.08 and 1.16 (3 H, two d, *J* 5 Hz, CH*Me*); *m/z* 286 (M^+, 1%), 271 (8), 242 (24), and 202 (Ph_2POH^+, 100) (Found: C, 71.0; H, 6.8; P, 10.5. $C_{17}H_{19}O_2P$ requires C, 71.3; H, 6.7; P, 10.8%).

2-*Diphenylphosphinoyl*-3-*ethyl*-3,4-*epoxypentane* (38p). In a similar way, ethyldiphenylphosphine oxide (2.1 g) in dry THF (30 ml), n-butyl-lithium (6.8 ml of 1.5M solution in hexane), and pentan-3-one gave the alcohol as needles (from EtOAc). Dehydration with TFA (20 ml) under reflux for 1 h gave, on work-up, the olefin (31; R^1 = R^3 = Me, R^2 = Et) (2.2 g). This crude material was treated with MCPBA (1.56 g) and sodium carbonate (0.77 g) in dichloromethane (60 ml) for 5 days. Work-up gave the white crystalline *epoxide* (38p) (2.26 g, 79% overall) as a mixture of isomers, R_F 0.36, δ ($CDCl_3$) 7.3—8.0 (10 H, m, Ph_2PO), 2.6—3.4 (1 H, several q, *J* 6 Hz, OCH), 1.9—2.5 (*ca.* 2 H, m, PCH and some $MeCH_2$), and 0.6—1.7 (*ca.* 10 H, m, remaining $MeCH_2$ and methyl signals); *m/z* 314 (M^+, 2%), 299 (6), 287 (12), 270 (11), 219 (7), and 202 (Ph_2POH^+, 100) (Found: M^+, 314.1455. $C_{19}H_{23}O_2P$ requires *M*, 314.1436).

1-*Diphenylphosphinoyl*-2-*methyl*-2,3-*epoxyheptane* (38o). Similarly, methyldiphenylphosphine oxide (2 g) in dry THF (30 ml), n-butyl-lithium (6.8 ml; 1.5M solution in hexane) and heptan-2-one gave a crude yellow product which was heated with TFA (25 ml) under reflux for 1 h. The mixture was evaporated under reduced pressure, taken up in chloroform (50 ml), washed with aqueous sodium hydrogen carbonate (3 × 25 ml), dried ($MgSO_4$), and evaporated to give the allyl phosphine oxide (31; R^1 = H, R^2 = Me, R^3 = Bu^n) as a mixture of geometrical isomers (*ca.* 2 : 1 by n.m.r.). Treatment with MCPBA and sodium carbonate (1 g) in dichloromethane (60 ml) for 20 h gave, after work-up and column chromatography (EtOAc), the *epoxide* (38o) (2 g, 66% overall), R_F 0.4, δ ($CDCl_4$), 7.3—8.0 (10 H, m, Ph_2PO), 2.96 (1 H, dd, J_{PH} 13 Hz and J_{AB} 15 Hz, PCH_2*), 2.5—2.8 (1 H, m, OCH), 2.29 (1 H, dd, J_{PH} 11 Hz and J_{AB} 15 Hz, PCH_2*), 1.42 (3 H, s, CMe), 1.1—1.5 [6 H, m, $(CH_2)_3$], and 0.85 (3 H, t, *J* 7 Hz, CH_2*Me*); *m/z* 328 (M^+, 1%), 312 (8), 271 (46), 242 (100), and 201 (Ph_2PO^+, 100) (Found: M^+, 328.1617. $C_{20}H_{25}O_2P$ requires *M*, 328.1592).

Rearrangements of Epoxides (38).—*Attempted rearrangement of epoxide* (38n). (a) *Using* BF_3·Et_2O). Epoxide (38n) (0.167 g) was stirred in dry ether (3 ml) under nitrogen with boron trifluoride–diethyl ether (0.2 ml). The mixture was stirred for 24 h and then poured into ether (20 ml), and washed with aqueous sodium hydrogen carbonate (20 ml), dried ($MgSO_4$), and evaporated to give a pale yellow gum (89 mg) consisting of five components by t.l.c. N.m.r. indicated a complex mixture of products and no starting material. No identifiable products were obtained.

(b) *Using* $LiClO_4$. Epoxide (38n) (100 mg) and lithium perchlorate (50 mg) were heated together in benzene under reflux in a Dean-Stark apparatus for 18 h. The mixture was poured into ether (50 ml), washed with brine (30 ml), dried ($MgSO_4$), and evaporated. N.m.r. indicated the presence of some unchanged epoxide in the mixture. Separation by preparative t.l.c. (EtOAc) was attempted but no pure materials could be isolated.

(c) *Using* LiBr. Epoxide (38n) (100 mg) and anhydrous lithium bromide were stirred together in dry THF (20 ml) for 4 days. Water (30 ml) was added and the mixture extracted with ether (4 × 30 ml); the organic solution was dried and evaporated to give unchanged (38n).

Treatment of epoxide (38m) *with* $TiCl_4$. A solution of epoxide (38 m) (200 mg) in dry dichloromethane (5 ml) was added to a stirred solution of titanium tetrachloride (0.1 ml) in dichloromethane (15 ml) under nitrogen at −78 °C. A yellow colour formed immediately. The mixture was stirred for 1 min and then poured into sodium hydrogen carbonate solution and extracted with ether (3 × 30 ml); the extract was dried and evaporated to give a gum which was separated by t.l.c. (EtOAc) into unchanged epoxide (99 mg, 50%) and a compound tentatively identified as 2-*chloro*-1-*diphenylphosphinoyl*-2,4-*dimethylpentan*-3-*ol* (39; R^1 = H, R^2 = Me, R^3 = Pr^i, X = Cl) (76 mg, 34%), a gum R_F 0.5, δ ($CDCl_3$) 7.4—8.0 (10 H, m, Ph_2PO), 4.73 (1 H, s, OH), 3.85 (1 H, d, J_{HH} 3 Hz, OC*H*^{i}Pr), 3.15 (1 H, dd, J_{PH} 13 Hz and J_{AB} 15 Hz, PCH_2*), 2.89 (1 H, dd, J_{PH} 9 Hz and J_{AB} 15 Hz, PCH_2*), 2.14 (1 H, d sept, *J* 3 Hz and 7 Hz, CHC*H*Me_2), 1.59 (3 H, d, J_{PH} 2 Hz, ClCMe), 1.05 and 0.98 (each 3 H, d, J_{HH} 7 Hz, CHMe_2*); *m/z* 315 (*M* − Cl, 2%), 309 and 307 (*M* − Pr^i, 2 and 5 respectively), 297 (4), 271 (12), and 202 (Ph_2POH^+, 100).

Treatment of epoxide (38j) *with* $MgBr_2$. Epoxide (38j) (200 mg) was added to a suspension of dry magnesium bromide (*ca.* 150 mg) in dry benzene and the mixture heated under reflux for 20 h. The mixture was cooled, poured into ether, filtered through Hyflo, washed with brine, dried, and evaporated to give a colourless gum tentatively identified as 2-*bromo*-1-*diphenylphosphinoyl*-2-*methylbutan*-3-*ol* (39; R^1 = H, R^2 = R^3 = Me, X = Br) (30 mg, 12%), R_F 0.45, δ ($CDCl_3$) 7.3—8.0 (10 H, m, Ph_2PO) 3.9—4.5 (1 H, br, OH), 4.25 (1 H, q, J_{HH} 7 Hz, C*H*Me), 2.6—3.1 (2 H, m, PCH_2*), 1.66 (3 H, d, J_{HH} 7 Hz, CH*Me*), and 1.35 (3 H, s, CMe); *m/z* 368 and 366 (M^+, each 2%), 353 and 351 (*M* − Me, each 7), 287 (*M* − Br, 13), 269 (64), 259 (94), 215 (27), and 201 (Ph_2PO^+, 100).

Treatment of epoxide (38m) *with* HCl. Epoxide (38m) (100 mg) and concentrated hydrochloric acid (0.5 ml) were stirred together in THF (5 ml) for 2.5 h, poured into ether (50 ml), washed with aqueous sodium hydrogen carbonate, dried, and evaporated to give a brown gum. N.m.r. and t.l.c. both confirmed the presence of a little starting material in the complex mixture. No other products were identified.

Treatment of epoxide (38m) *with* TsOH. Epoxide (38m) (200 mg) and TsOH (100 mg) were heated together in benzene under reflux in a Dean-Stark apparatus for 1.5 h by which time all the starting material had been consumed. The mixture was poured into ether (30 ml), washed with aqueous sodium hydrogen carbonate (3 × 25 ml), dried, and evaporated to a gum). The main component was separated by column chromatography (EtOAc) as a colourless gum (174 mg), but could not be identified. No ketones were present.

Treatment of Epoxide (38m) *with* TFA. Epoxide (38m) (74 mg) was kept at 34 °C in solution in TFA (1 ml) for 20 h and then poured into chloroform (40 ml) and potassium carbonate (2 spatula ends). The inorganic solids were filtered off and the solution evaporated to give a gum which was separated by preparative t.l.c. (EtOAc) into two components, tentatively identified as 2-(*diphenylphosphinoylmethyl*)-2,3-*dimethylbutyraldehyde* (40) (27 mg, 36.5%), m.p. 104—110 °C (from EtOAc), R_F 0.4, $\nu_{max.}$ (CCl_4) 1 718 (C=O), 1 434 (P–Ph), and 1 170 cm^{-1} (P=O); δ ($CDCl_3$) 9.58 (1 H, s, CHO), 7.3—8.0 (10 H, m, Ph_2PO), 2.78 (1 H, dd, J_{PH} 12 Hz and J_{AB} 15 Hz, PCH_2*), 2.44 (1 H, dd, J_{PH} 10 Hz and J_{AB} 15 Hz, PCH_2*), 2.04 (1 H, sept, J_{HH} 7 Hz, C*H*Me_2), 11.1 (3 H, s, CMe), and 0.84 and 0.80 (3 H, each, d, J_{HH} 7 Hz, CH*Me*$_2$*); *m/z* 314 (M^+, 6%), 299 (6), 285 (47), 259 (83), 230 (51), 215 [$Ph_2P(O)CH_2$, 100], and 201 (Ph_2PO^+, 100); and 1-*diphenylphosphinoyl*-2,4-*dimethylpentan*-3-*one* (3m) (32 mg, 43%), a gum, R_F 0.3, $\nu_{max.}$ (CCl_4) 1 702 (C=O), 1 434 (P–Ph), and 1 168 (P=O); δ ($CDCl_3$) 7.4—8.0 (10 H, m, Ph_2PO), 2.0—3.6 (3 H, m, PCH_2*C*H*Me), 2.68 (1 H, sept, J_{HH} 7 Hz, C*H*Me_2), 1.23 (3 H, d, J_{HH} 7 Hz, CH*Me*), and 0.84 and 1.04 (each 3 H, d, J_{HH} 7 Hz, CH*Me*$_2$*).

Treatment of Epoxide (38p) *with* TFA.—Epoxide (38p) (100 mg) was heated in TFA (5 ml) under reflux for 1 h after which the solution was evaporated. The residue was taken up in chloroform (25 ml) and the solution washed with aqueous sodium hydrogen carbonate (2 × 25 ml) and then dried, and evaporated to give a gum. This was separated by preparative t.l.c. (EtOAc) into an unidentified gum (22 mg) which showed no carbonyl absorption in the i.r. and a gum (60 mg) which may have contained the two diastereoisomers of 2-diphenylphosphinoyl-3-ethylpentan-4-one (3p), R_F 0.3, $\nu_{max.}$ ($CHCl_3$) 1 709 (C=O), 1 348 (P–Ph), and 1 173 (P=O); δ ($CDCl_3$) 7.3—8.0 (10 H, m, Ph_2PO) and 1.96 and 2.24 (each 3 H, s, COMe), remaining signals not unequivocably assignable, in a mixture with other unidentified products.

Treatment of epoxide (38j) *with* TFA. Epoxide (38j) (50 mg) in solution in TFA (0.5 ml) was kept at 34 °C for 24 h and then poured into a suspension of potassium carbonate in chloroform; the resulting solution was dried ($MgSO_4$) and evaporated to give, after preparative t.l.c. (EtOAc), the ketone (3j) (46 mg, 92%), identical with the compound prepared previously.

Treatment of epoxide (38j) *with* TsOH. Epoxide (38j) (200 mg) and TsOH (100 mg) were heated together in benzene (3 ml) under reflux for 1 h. The solution was poured into ether (30 ml), washed with aqueous sodium hydrogen carbonate (3 × 25 ml), dried, and evaporated. Preparative t.l.c. (EtOAc), gave the ketone (3j) (104 mg, 52%), again identical with authentic material.

Attempted rearrangement of the epoxide (38i) (*Table* 4). The epoxide (38i) (500 mg, 1.6 mmol) was stirred overnight in TFA (10 ml) at room temperature and under nitrogen. The solution was poured onto solid K_2CO_3 (5 g), water added (100 ml), and the mixture extracted with chloroform (3 × 25 ml). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (2 × 25 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give an oil. P.l.c. on silica (eluted with EtOAc), gave the ketone (3i) (150 mg, 30%), together with the *diol* (42) (266 mg, 50%) as needles, m.p. 125—128 °C (from EtOAc), R_F 0.33 (EtOAc), δ ($CDCl_3$) 1.04—2.04 (8 H, m, ring CH_2's), 2.56 (1 H, dd, $J_{H_AH_B}$ 16 Hz, J_{HP} 9 Hz, PCH_AH_B), 2.94 (1 H, dd, $J_{H_AH_B}$ 16 Hz, J_{PH_B} 13 Hz, PCH_AH_B), 3.52 (1 H, m, C*H*OH), 4.24 (2 H, br s, OH), and 7.30—7.96 (10 H, m, Ph_2PO); $\nu_{max.}$ 3 360 (O–H), 1 435 (P–Ph), and 1 160 cm^{-1} (P=O); *m/z* 330 (M^+, 6%), 312 ($M - H_2O$, 5), 202 (Ph_2POH^+, 100), and 201 (Ph_2PO^+, 29) (Found: M^+, 330.1380. $C_{19}H_{23}O_3P$ requires *M*, 330.1384).

The diol rearranged to the ketone (3i) in 60% yield when heated under reflux in TFA for 18 h and worked up as above.

The epoxide (38i) also gave the ketone (3i) with TsOH in benzene under reflux for 18 h as the major product in 40% yield after p.l.c.

Reaction of the epoxide (38i) with boron trifluoride–ether complex in dichloromethane at 0 °C for 6 h also gave the ketone (3i) in 40% yield after p.l.c.

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