Synthesis of Single Isomers (*E* or *Z*) of Unsaturated Carboxylic Acids by the Horner-Wittig Reaction

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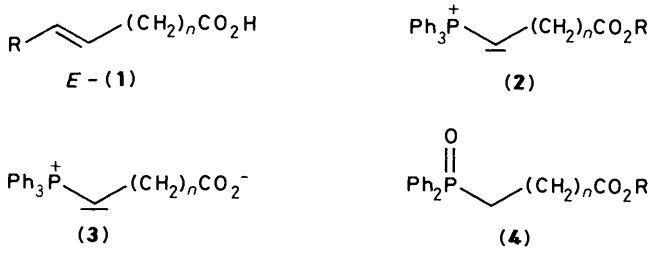
Alkyl(diphenyl)phosphine oxides (**5**) are used to synthesize pure *E* or *Z* isomers of unsaturated acids. The keto acids (**10**), made by two routes, are reduced to hydroxy acids whose crystalline lactones (**12**) can be separated and purified. Stereospecific elimination of $Ph_2PO_2^-$ gives the unsaturated acids.

Both Wittig routes[1] to unsaturated acids (**1**) have been used in the past: phosphonium ylides react with $RO_2C(CH_2)_nCHO$ to give esters of *Z*-(**1**) and ylides with a terminal ester (**2**) or carboxylate anion group (**3**) react with aldehydes, again with *Z*-selectivity. This latter route is important in prostaglandin synthesis[2] but ylides (**2**) or (**3**) (n = 1,2,3) cannot be used because of side-reactions.[3] All these methods produce mixtures, usually rich in the *Z*-isomer, and some progress has been made in reversing the selectivity by variation of base and solvent, at least with aromatic aldehydes,[4] but mixtures still result. We report[5] that the Horner-Wittig reaction[6] may be used to make unsaturated acids (**1**) with variable stereoselectivity but that separation of crystalline phosphine oxide intermediates leads to pure samples of *E* or *Z* products (**1**) with reasonable material conversion.

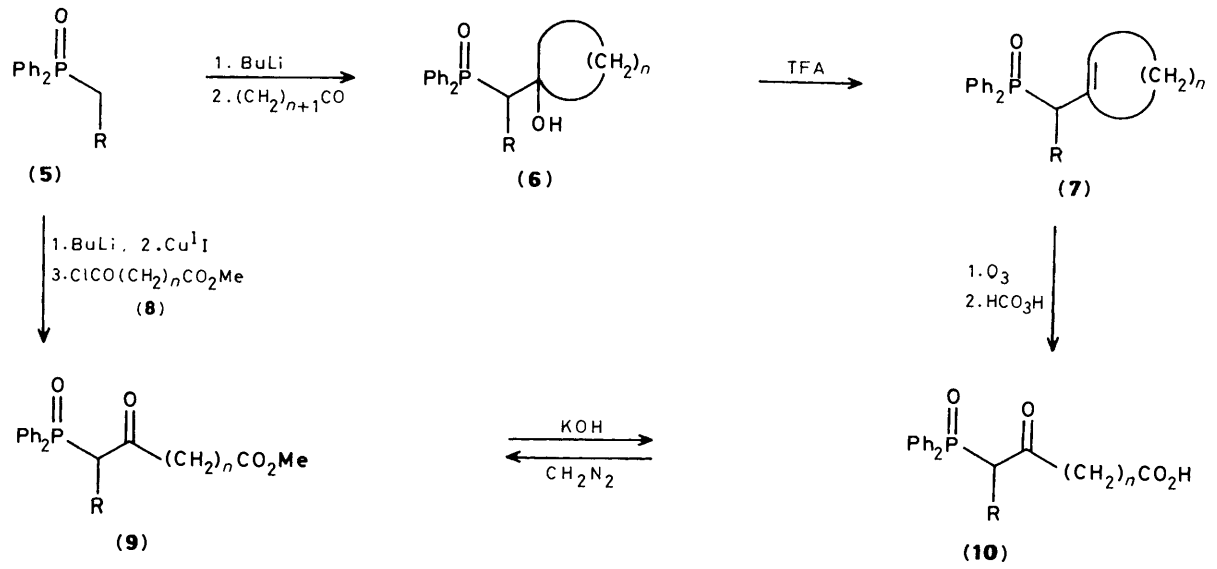
Mono-, di-, or even tri-anions of the phosphine oxides (**4**) gave unsatisfactory reactions with aldehydes, and we used the alternative approach of reduction of the α-diphenylphosphinoyl ketones[6] (**10**). These keto acids (**10**) were made by two routes, oxidative cleavage of the cyclic alkenes (**7**), derived from the tertiary alcohols (**6**) by acid-catalysed dehydration[7] (Table 1), or, preferably, by acylation of the copper derivatives of phosphine oxides (**5**) with the ester acid chlorides (**8**) (Table 2). Acylation with cyclic anhydrides or *e.g.* dimethyl succinate gave lower yields, probably because of proton transfer. The oxidative cleavage route is satisfactory for (**7**; n = 3—5) but smaller rings are not so easily made,[8] and larger rings give lower yields (n = 10 in Table 1). One keto ester (**9i**) with an extra double bond and therefore not available by oxidative cleavage was made by alkylation of (**9b**) with cinnamyl bromide.

Reduction of Keto Acids (**10**).—Reduction of α-diphenylphosphinoyl ketones is normally *threo*-selective[6] but functional groups in either side-chain can reduce this selectivity.[9] The keto acids (**10**) and esters (**9**) were reduced with low *threo*-selectivity (Table 3), the best conditions being sodium borohydride at room temperature in ethanol which had been passed through alumina to remove traces of acid. The hydroxy acids (**11**) or their esters were poorly crystalline and difficult to separate into diastereoisomers, but the crystalline lactones (**12**) were more easily handled and could be separated into pure diastereoisomers by flash chromatography.[10]

A comparison of lactonisation procedures (Table 4) showed that acid (TsOH, toluene, or TFA) treatment of the hydroxy esters derived by reduction of keto esters (**10**) without purification gave the best yields. We confirmed that our lactonization procedure avoided epimerisation at either chiral



(**1**) (**2**) (**3**) (**4**)



(**5**) (**6**) (**7**) (**8**) (**9**) (**10**)

Scheme 1.

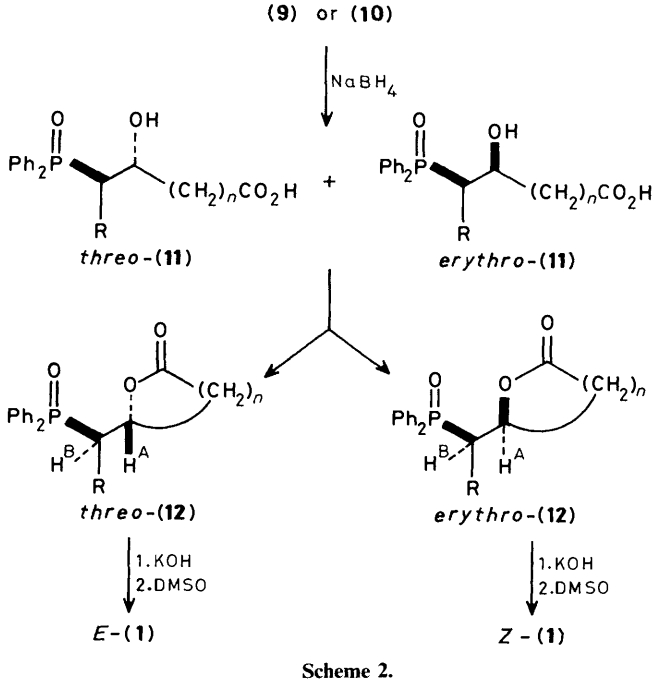
Table 1. Oxidative cleavage of allylic phosphine oxides

Entry	R	*n*	Yield (6) (%)	Yield (7) (%)	Oxidative cleavage Method[a]	Product	Yield (%)
a	$C_{14}H_{29}$	3	77	75	A	(**10a**)	92
b	H	4	87	94	B	(**9b**)	65
c	Me	4	80	83	A	(**9c**)	64
					B	(**9c**)	62
					C	(**10c**)	*ca.* 89[b]
					D	*c*	*c*
d	$C_{13}H_{27}$	4	81	55			
e	Me	6	50	85			
f	Me	10	15				

[a] Methods: A; $NaIO_4$, RuO_2, B; 1. O_3, 2. HCO_3H, C; 1. O_3, 2. Jones reagent, D; 1. O_3, 2. H_2O_2 or HIO_4, or 1. O_3, 2. Me_2S, 3. NaOCl, or O_3, silica gel, or $NaIO_4$, $KMnO_4$. [b] Product contaminated with Cr^{III} impurities. [c] No reaction or poor yield.

Table 2. Acylation of phosphine oxides (**5**) to give keto esters (**9**)

Starting material R in (**5**)	Base	Acylating agent *n*	Acylating agent Reagent	Keto ester Compd.	Keto ester Yield (%)
Me	BuLi	2	Anhydride	(**10g**)	*ca.* 36
	BuLi	2	Methyl ester	(**9g**)	27
	1. BuLi 2. $Cu^{I}I$	2	(**8**; *n* = 2)	(**9g**)	60
C_5H_{11}	1. BuLi 2. $Cu^{I}I$	2	(**8**; *n* = 2)	(**9h**)	73
Me	1. BuLi 2. $Cu^{I}I$	4	(**8**; *n* = 4)	(**9c**)	79
(**9b**)	K_2CO_3, PhCH=CNBr			(**9i**)	61



Scheme 2.

centre by hydrolysis of a pure sample of *erythro*-(**12c**) to give the hydroxy acid *erythro*-(**11c**) and recyclisation to *erythro*-(**12c**) with TsOH in refluxing toluene. Though the *erythro* series is less stable than the *threo*, the regenerated lactone (**12c**) was free from *threo*-(**12c**) by n.m.r. and chromatography. From Mukaiyama's[11] 2-chloro-1-methylpyridinium salt method, only *threo*-(**12c**) could be isolated from a 59:41 *threo*:*erythro* mixture of the methyl ester of (**11c**).

Table 3. Synthesis of unsaturated acids (**1**) from keto acids (**10**)

Starting material Compd.	R	*n*	*erythro*: *threo*	Yield of products (%) *erythro*- (**12**)	*Z*-(**1**)	*threo*- (**12**)	*E*-(**1**)
(**9a**)	C_4H_{19}	3	35:65	8	55	51	88
(**9c**)	Me	4	23:77	19	91	63	93
(**9h**)	C_5H_{11}	2	43:57	*a*	55	*a*	73

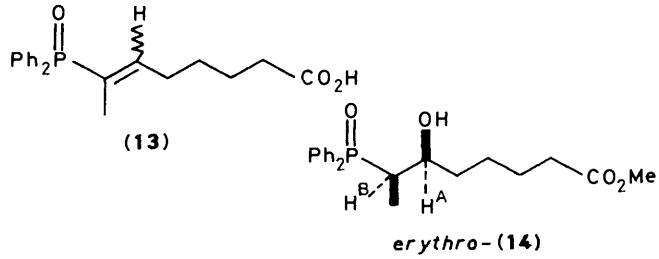
[a] Separated by h.p.l.c., combined yield 84%.

Table 4. Lactonisation of hydroxy acids (**11**) and esters

Starting material[a]	Reagent	Product	Yield (%)
(**10a**)	TFAA, benzene, 7 °C[b]	(**12a**)	59
	TFA[b]	(**12a**)	49
(**9c**)	TsOH, toluene, reflux	(**12c**)	82
(**9c**)	1. Im_2CO, Et_3N, 2. DBU[c]	(**12c**)	76
(**9c**)	TFAA, benzene, 8 °C[b]	(**12c**)	54
(**9c**)	MeClP[d]	*threo*-(**12c**)	68
(**9c**)	DBU,[c] THF	*e*	
(**10c**)	DCC, DMAP[f]	*e*	
	Ph_3P, DEAD[g]	*e*	
(**9h**)	TFA[b]	(**12h**)	84

[a] Reduction and lactonisation were carried out without isolation of (**11**) or its methyl ester. [b] TFA is trifluoroacetic acid, TFAA is the anhydride, see W. Bakler, W. D. Ollis, and T. S. Zealley, *J. Chem. Soc.*, 1952, 1447; K. C. Nicolaou, *Tetrahedron*, 1977, **33**, 683; D. Taub, N. N. Girotra, R. D. Hoffsommer, C. H. Kuo, H. L. Slates, S. Weber, and N. L. Wendler, *Tetrahedron*, 1968, **24**, 2443. [c] Im is imidazole, DBU is 1,5-diazabicyclo[5.4.0]undec-5-ene, see H. A. Staab and A. Mannschreck, *Chem. Ber.*, 1962, **95**, 1284; E. W. Colvin, T. A. Purcell, and R. A. Raphael, *J. Chem. Soc., Perkin Trans. 1*, 1976, 1718. [d] Intermediates was 59:14 *threo*:*erythro* MeClP is 1-methyl-2-chloropyridinium iodide, see ref. 11. [e] No product isolated. [f] DCC is dicyclohexylcarbodi-imide, DMAP is 4-*N*,*N*-dimethylaminopyridine, M. Smith, J. G. Moffat, and H. G. Khorana, *J. Am. Chem. Soc.*, 1958, **80**, 6204. [g] DEAD is diethyl azodicarboxylate, see O. Mitsunobu, *Synthesis*, 1981, 1; B. R. Castro, *Org. React. (N.Y.)*, 1983, **29**, 1.

Completion of the Horner-Wittig Reaction on the Lactones (**12**).—The usual conditions[6] for completing the Horner-Wittig reaction are a sodium or potassium base in a dipolar aprotic solvent (NaH in DMF or KOH in DMSO). The lactone (**12c**) gave the vinyl phosphine oxide (**13**) with NaOMe in DMF, base-catalysed elimination being preferred to nucleophilic attack at the lactone. Other bases (NaOH, KOH, K_2CO_3) in hydroxylic solvents (MeOH, H_2O/THF) did cleave the lactones to regenerate the hydroxy acids (**11**) on acidic work-up, but these compounds foam on drying, and the hydroxy acids (**11**; *n* = 2) are prone to relactonise during acidic work-up.



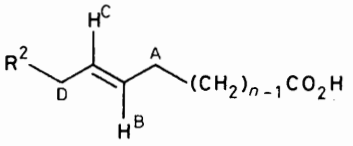
The most convenient procedure was hydrolysis of the lactones (**12**) with a roughly four-fold excess of KOH in aqueous THF and removal of the solvent by freeze-drying. The solid

Table 5. Assignment of stereochemistry (Scheme 2)

			erythro					*threo*				
Compd.	R	*n*	$H_A(\delta)$	J_{AP}(Hz)	$H_B(\delta)$	J_{BP}(Hz)	J_{AB}(Hz)	$H_A(\delta)$	J_{AP}(Hz)	$H_B(\delta)$	J_{BP}(Hz)	J_{AB}(Hz)
(**14**)	Me	4	4.01	*a*	2.34	7.3	0.9	3.82	*a*	2.67	10.7	7.4
(**12a**)	$C_{14}H_{29}$	3	4.67	17.0	2.69	8.0	4.0	4.52	11.7	2.60	13.0	2.6
(**12c**)	Me	4	*ca.* 4.85	*a*	*ca.* 2.65	*a*	*a*	4.43	9.0	2.90	9.8	2.5
(**12h**)	C_5H_{11}	2	4.86	11.6	*ca.* 2.67	*a*	8.1	*ca.* 4.75	*a*	2.93	10.0	3.8

[a] Could not be measured.

Table 6. Stereochemistry of unsaturated acids (**15**) [= (**1**; R = R^2CH_2)]



(**15**)

Acid	R^2	*n*	J_{BC}[a] (Hz)	C_A[b] (δ)	C_D[b] (δ)	$\nu_{max.}$[c]
Z-(**15a**)[d]	$C_{13}H_{27}$	3	10.8			
Z-(**15c**)[e]	H	4	10.9[f]			720
Z-(**15h**)[g]	C_4H_9	2	10.8	27.21	22.94	920
E-(**15a**)[h]	$C_{13}H_{27}$	3	15.0			980
E-(**15c**)[e]	H	4	15.2			975
E-(**15h**)[i]	C_4H_9	2	15.4	32.43	27.97	985

[a] 400 MHz ^{1}H N.m.r. spectrum. [b] 62.9 MHz ^{13}C N.m.r. spectrum, *cf.*, A. Barabas, A. A. Botar, A. Gocan, N. Popovici, and F. Hodosan, *Tetrahedron*, 1978, **34**, 2191. [c] HC=CH Out-of-plane deformation. [d] Isolated from *Limanthes douglasii* and identified by absence of *trans* i.r. band, see ref. 21. [e] Synthesized and identified by i.r. bands, see ref. 20. [f] Observed by irradiation of vinylic Me. [g] Synthesized but no details given, T. Fujisawa, T. Sato, T. Kuwara, and K. Naruse, *Chem. Lett.*, 1980, 1123; the methyl ester has also been synthesized, H. Sprecher, *Lipids*, 1968, **3**, 14. [h] Prepared by photolysis of *Z*-(**15a**), R. N. Young, W. Coombs, Y. Guindon, J. Rokach, D. Ethier, and R. Hall, *Tetrahedron Lett.*, 1981, **22**, 4933; the i.r. spectrum has been reported, A. Mitcham, A. V. Bailey, and V. W. Tripp, *J. Am. Oil Chem. Soc.*, 1973, **50**, 446. [i] Prepared by the Ireland-Claisen rearrangement and the low-field n.m.r. (J_{BC} could not be determined) and i.r. spectra reported, R. E. Ireland, R. H. Mueller, and A. K. Willard, *J. Am. Chem. Soc.*, 1976, **98**, 2868.

mixture of KOH and the potassium salt of (**11**) was dissolved in dry DMSO at 50 °C for 1 h. This gave good yields of *E*-(**1**) from *threo*-(**12**) (Table 3) and moderate yields of *Z*-(**1**) from *erythro*-(**12**). Each sample of acid was free from the other by g.l.c. of the methyl esters.

Assignment of Stereochemistry.—The stereochemistry of Horner-Wittig intermediates can normally be assigned from their ^{1}H n.m.r. spectra.[12] These correlations work well for the hydroxy esters, *e.g.* (**14**), Table 5 (J_{AB} is small for the *erythro* and large for the *threo* isomer). However, the lactones (**12**) have different but consistent trends (Table 5), *e.g.* J_{AB} is larger for the *erythro* isomer. These assignments are confirmed by the stereochemistry of the unsaturated acids (**1**) derived from their lactones (**12**) by the stereospecific *syn* elimination[12] of $Ph_2PO_2^-$ (Table 6), and by *X*-ray crystal structures of related compounds.[13]

Conclusions.—These simple examples show that the three-stage synthesis (i), acylation of the copper derivative of phosphine oxides, (ii) reduction, lactonisation, and separation of the lactones (**12**), and (iii) hydrolysis and elimination gives pure samples of *E*- and *Z*-unsaturated acids (**1**) in reasonable yield. The material conversion into *E*-acids (**1**) is higher than that for the *Z*-acids, but we have an alternative[13] *erythro*-selective synthesis of the lactones (**12**) from the same phosphine oxides (**5**).

Experimental

BuLi refers to butyl-lithium, THF to tetrahydrofuran dried from potassium, DMSO to dimethyl sulphoxide dried over 3 Å molecular sieves, and DMF to dimethylformamide. Protons marked with an asterisk in the n.m.r. spectra are diastereotopic.

Diphenyltetradecylphosphine Oxide (**1**; R = n-$C_{13}H_{27}$).—Triphenylphosphine (47.2 g, 0.18 mol), 1-bromotetradecane (50 g, 0.18 mol), and dry toluene (10 ml) gave the phosphonium salt after 24 h and thence, after hydrolysis, the *phosphine oxide* (35.2 g, 49%), m.p. 73—74 °C (from hexane) (Found: C, 78.3; H, 9.95; P, 7.7. $C_{26}H_{39}OP$ requires C, 78.4; H, 9.85; P, 7.8%); R_F(Et_2O) 0.21; $\nu_{max.}$($CHCl_3$ solution) 1 440 (PhP) and 1 170 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.4 (10 H, m, Ph_2PO), 2.4—2.1 (2 H, m, PCH_2), 1.6—1.1 [24 H, m, $(CH_2)_{12}Me$], and 0.85 (3 H, t, *J* 6 Hz, Me); *m/z* 398 (10%, M^+), 216 (71, $Ph_2POHCH_2^+$), 215 (70, $Ph_2POCH_2^+$), 202 (100, Ph_2POH^+), and 201 (43, Ph_2PO^+).

Pentadecyldiphenylphosphine Oxide (**1**; R = n-$C_{14}H_{29}$).—Triphenylphosphine (21.4 g, 81.6 mmol), 1-bromopentadecane (23.8 g, 81.7 mmol), and dry toluene (15 ml) gave the phosphonium salt (38.25 g) and thence, after hydrolysis, the *phosphine oxide* (27.0 g, 80%), m.p. 83—83.5 °C (from hexane–EtOAc) (Found: C, 78.6; H, 9.9. $C_{27}H_{41}OP$ requires C, 78.6; H, 10.0%); R_F(EtOAc) 0.39; $\nu_{max.}$(Nujol mull) 1 436 (PhP) and 1 188 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.4 (10 H, m, Ph_2PO), 2.45—2.0 (2 H, m, PCH_2), 1.9—1.0 [26 H, m, $(CH_2)_{13}Me$], and 0.88 (3 H, t, *J* 6 Hz, Me); *m/z* 412 (6%, M^+), 216 (68, $Ph_2POHCH_2^+$), 215 (84, $Ph_2POCH_2^+$), 202 (100, Ph_2POH^+), and 201 (45, Ph_2PO^+).

1-(1-*Diphenylphosphinoyltetradecyl*)*cyclohexanol* (**6d**).—In the same way as before,[7] BuLi (1.55M solution in hexane; 16.1 ml, 25 mmol), the phosphine oxide (**5**; R = n-$C_{13}H_{27}$) (9.95 g, 25 mmol) in THF (250 ml), and cyclohexanone (2.84 g, 29 mmol) in THF (3 ml) gave the *alcohol* (10 g, 81%), m.p. 117—121 °C (from hexane–EtOAc) (Found: C, 77.4; H, 9.9; P, 6.3. $C_{32}H_{49}O_2P$ requires C, 77.4; H, 9.95; P, 6.2%); R_F(Et_2O) 0.49; $\nu_{max.}$($CHCl_3$) 3 380 (OH), 1 440 (PhP), and 1 168 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.3 (10 H, m, Ph_2PO), 3.24 (1 H, s, OH), 2.24 (1 H, ddd, J_{PH} 8.8, J_{HH} 4.5 and 1 Hz, PCH), 2.1—0.7 (34 H, m, methylene protons), and 0.87 (3 H, t, *J* 5.8 Hz, Me); *m/z* 496 (11%, M^+), 478 (18, $M^+ - H_2O$), 229 (33), 216 [25, $Ph_2P(OH)CH_2^+$], 215 [20, $Ph_2P(O)CH_2^+$], 202 (100, Ph_2POH^+), and 201 (48, Ph_2PO^+).

1-(1-*Diphenylphosphinoylpentadecyl*)*cyclopentanol* (**6a**).—In the same way, BuLi (1.55M solution in hexane; 5.3 ml, 8.2 mmol), the phosphine oxide (**5**; R = n-$C_{14}H_{29}$) (3.22 g, 7.8 mmol), and cyclopentanone (0.72 g, 8.6 mmol) gave the *alcohol* (2.97 g, 77%), m.p. 99—102 °C (from diethyl ether–hexane) (Found: C, 77.5; H, 10.15. $C_{32}H_{49}O_2P$ requires C, 77.4; H, 9.95%); R_F(Et_2O) 0.63; $\nu_{max.}$(Nujol mull) 3 400 (OH), 1 445 (PhP), and 1 160 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.3 (10 H, m, Ph_2PO), 4.7 (1 H, s, OH), 2.35—2.05 (1 H, m, PCH), 2.1—0.7 (34 H, m, methylene protons), and 0.85 (3 H, t, *J* 6 Hz, Me); *m/z* 496 (9%, M^+), 478 (15, $M^+ - H_2O$), 313 (46), 258 (30), 202 (100, Ph_2POH^+), and 201 (51, Ph_2PO^+).

1-(1-*Diphenylphosphinoylethyl*)*cyclo-octanol* (**6e**).—BuLi (1.55M solution in hexane) was added dropwise to a stirred solution of the phosphine oxide[14] (**5**; R = Me) (1 g, 4.35 mmol) in THF under nitrogen at 0 °C, until the orange colour persisted. Further BuLi (1.55M solution in hexane; 2.95 ml, 4.57 mmol) was added dropwise at 0 °C after which the dark red solution was cooled to −70 °C, and a solution of cyclo-octanone (0.604 g, 4.79 mmol) in dry THF (5 ml) was added dropwise over 10 min. The mixture was allowed to warm to room temperature over *ca.* 1 h, when saturated aqueous ammonium chloride (20 ml) was slowly added, and the bulk of the THF was removed by evaporation under reduced pressure. Water (50 ml) was added and the mixture was extracted with dichloromethane (3 × 40 ml). The combined organic extracts were washed with water (25 ml) and saturated brine (20 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by flash column chromatography[10] on Merck 9385 silica gel (95 g; 3.5 cm diam. × 15.2 cm) eluting with hexane–EtOAc (1:3) to give the *alcohol* (0.77 g, 50%), m.p. 190—192 °C (Found: C, 74.45; H, 8.2. $C_{22}H_{29}O_2P$ requires C, 74.15; H, 8.2%); R_F(EtOAc) 0.5; $\nu_{max.}$($CHCl_3$) 3 380 (OH), 1 440 (PhP), and 1 160 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.3 (10 H, m, Ph_2PO), 2.67 (1 H, dq, J_{PH} 8.6 and J_{HH} 7.6 Hz, PCH), 2.1—0.8 [14 H, m, $(CH_2)_7$], and 1.12 (3 H, dd, J_{HH} 7.55 and J_{PH} 17.9 Hz, PCH*Me*); *m/z* 356 (8%, M^+), 338 (4, $M^+ - H_2O$), 230 [51, $Ph_2P(OH)CHMe^+$], 229 [30, $Ph_2P(O)CHMe^+$], 202 (100, Ph_2POH^+), and 201 (57, Ph_2PO^+).

1-(1-*Diphenylphosphinoylethyl*)*cyclododecanol* (**6f**).—In the same way, BuLi (1.55M solution in hexane), the phosphine oxide (**5**; R = Me) (1 g, 4.35 mmol) in THF gave the *alcohol* (0.26 g, 15%), m.p. 171—172.5 °C (Found: C, 75.8; H, 9.25; P, 7.3. $C_{26}H_{37}O_2P$ requires C, 75.7; H, 9.05; P, 7.5%); R_F(EtOAc) 0.49; $\nu_{max.}$($CHCl_3$) 3 390 (OH), 1 438 (PhP), and 1 168 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.3 (10 H, m, Ph_2PO), 4.66 (1 H, s, OH), 2.59 (1 H, quint., *J* 7.8 Hz, PCH), 1.9—0.7 [22 H, m, $(CH_2)_{11}$], and 1.11 (3 H, dd, J_{HH} 7.6 and J_{PH} 17.9 Hz, PCH*Me*); *m/z* 412 (7%, M^+), 394 (12, $M^+ - H_2O$), 230 [57, $Ph_2P(OH)CHMe^+$], 229 [26, $Ph_2P(O)CHMe^+$], 202 (100, Ph_2POH^+), and 201 (57, Ph_2PO^+).

1-(1-*Diphenylphosphinoyltetradecyl*)*cyclohexene* (**7d**).—Our previously reported method[7] on the alcohol (**6d**) (7.44 g, 15 mmol) gave the *allylphosphine oxide* (3.91 g, 55%), m.p. 103—104 °C (from hexane) (Found: C, 80.4; H, 9.65; P, 6.7. $C_{32}H_{47}OP$ requires C, 80.3; H, 9.9; P, 6.5%); R_F(Et_2O) 0.35; $\nu_{max.}$($CHCl_3$) 1 441 (PhP) and 1 176 cm^{-1} (P=O); δ($CDCl_3$) 8.0—6.9 (10 H, m, Ph_2PO), 5.35 (1 H, m, C=CH), 3.0—2.4 (1 H, m, PCH), 2.3—1.3 (4 H, m, CH_2C=$CHCH_2$), 1.7—0.5 [28 H, m, $CH_2(CH_2)_2CH_2$ and $(CH_2)_{12}$], and 0.85 (3 H, t, *J* 6 Hz, Me), *m/z* 478 (12%, M^+), 296 (12), 216 [10, $Ph_2P(OH)CH_2^+$], 215 [11, $Ph_2P(O)CH_2^+$], 203 [42, $Ph_2P(OH)H^+$], 202 (100, Ph_2POH^+), and 201 (36, Ph_2PO^+).

1-(1-*Diphenylphosphinoylpentadecyl*)*cyclopentene* (**7a**).—In the same way the alcohol (**6a**) (6.16 g, 12.4 mmol) gave the *allylphosphine oxide* (4.45 g, 75%), m.p. 110—114.5 °C (from diethyl ether) (Found: C, 80.3; H, 10.0. $C_{32}H_{47}OP$ requires C, 80.3; H, 9.9%); R_F(Et_2O) 0.36; $\nu_{max.}$(Nujol mull) 1 440 (PhP) and 1 180 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.2 (10 H, m, Ph_2PO), 5.4 (1 H, m, C=CH), 3.1 (1 H, ddd, J_{PH} 12, J_{HH} 9 and 3.5 Hz, PCH), 2.15 (4 H, m, CH_2C=$CHCH_2$), 1.7 (2 H, m, homoallylic CH_2), 1.5—0.9 [26 H, m, $(CH_2)_{13}$], and 0.85 (3 H, t, *J* 6 Hz, Me); *m/z* 478 (79%, M^+), 201 [40, $Ph_2P(OH)H^+$], 202 (100, Ph_2POH^+), and 201 (47, Ph_2PO^+).

1-(1-*Diphenylphosphinoylethyl*)*cyclo-octene* (**7e**).—A solution of the alcohol (**6e**) (0.77 g, 2.16 mmol) in trifluoroacetic acid (30 ml), under nitrogen, was heated under reflux for 30 min, cooled, and the bulk of the trifluoroacetic acid removed by evaporation under reduced pressure. Water (45 ml) was added and the mixture was extracted with ethyl acetate (3 × 25 ml). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (20 ml), water (20 ml), and saturated brine (15 ml), dried, (Na_2SO_4) and evaporated under reduced pressure. The residue was recrystallised from ethyl acetate–hexane to give the *allylphosphine oxide* (0.62 g, 85%), m.p. 152—153 °C; R_F(EtOAc) 0.44; $\nu_{max.}$ 1 440 (PhP) and 1 174 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.3 (10 H, m, Ph_2PO), 5.63 (1 H, dt, *J* 4.1 and 8.2 Hz, C=CH), 3.03 (1 H, quint., *J* 7.6 Hz, PCH), 2.5—1.7 (4 H, m, cyclo-octene allylic protons), 1.8—1.1 [8 H, m, $CH_2(CH_2)_4CH_2$], and 1.34 (3 H, dd, J_{HH} 7.3 and J_{PH} 16.4 Hz, PCH*Me*) (Found: M^+, 338.1807. $C_{22}H_{27}OP$ requires M^+, 338.1800); *m/z* 338 (15%, M^+), 230 [15, $Ph_2P(OH)CHMe^+$], 203 [26, $Ph_2P(OH)H^+$], 202 (100, Ph_2POH^+], and 201 (34, Ph_2PO^+). The simplicity of the spectra suggests the presence of only one geometrical isomer (presumably the less strained, thermodynamically more favourable *E*-isomer).

1-(1-*Diphenylphosphinoylethyl*)*cyclododecene* (**7f**).—In the same way the alcohol (**6f**) (0.2 g; 0.48 mmol) gave the *allylphosphine oxide* as a colourless gum, R_F[light petroleum (b.p. 40—60 °C)–EtOAc (3:7)] 0.38; $\nu_{max.}$ 1 440 (PhP) and 1 170 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.2 (10 H, m, Ph_2PO), 5.73 (1 H, dt, *J* 3.9 and 7.3 Hz, C=CH), 2.95 (1 H, quint., *J* 7.5 Hz, PCH), 2.3—1.7 (4 H, m, cyclododecene allylic protons), 1.8—0.8 [19 H, m, $CH_2(CH_2)_8CH_2$ and Me] (Found: M^+, 394.2448. $C_{26}H_{35}OP$ requires M^+, 394.2426); *m/z* 394 (7%, M^+), 203 [25, $Ph_2P(OH)H^+$], 202 (100, Ph_2POH^+), and 201 (34, Ph_2PO^+). The simplicity of the spectrum again suggests the presence of only one geometrical isomer.

Methyl 7-*Diphenylphosphinoyl*-6-*oxoheptanoate* (**9b**).—Following the method of Sharpless,[15] water (25 ml) was added to a stirred solution of the allylphosphine oxide[7] (**7b**) (1.48 g, 5 mmol) in carbon tetrachloride (15 ml) and acetonitrile (15 ml). The mixture was cooled to 16 °C, sodium periodiate (4.39 g, 20.5 mmol) and then ruthenium dioxide hydrate (50 mg, 0.38 mmol) were added, and the mixture was stirred vigorously for 2.5 h with cooling to maintain the temperature at 16—18 °C. Water (50 ml) was added and the mixture was extracted with dichloromethane (3 × 30 ml). The combined organic extracts were washed with dilute hydrochloric acid (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give a black gum. This was dissolved in EtOAc (100 ml) and the solution was washed with saturated brine (50 ml), dried (Na_2SO_4), refiltered through Celite and evaporated under reduced pressure to give a purple gum. A 3% solution of hydrogen chloride in methanol[16] (100 ml), prepared by cautious dropwise addition of acetyl chloride (5 ml) to methanol (95 ml), was added to the gum and the mixture was stirred at room temperature for 18 h. Solvent was removed by evaporation under reduced pressure, EtOAc (75 ml) was added, and the solution was washed with water (20 ml), saturated

aqueous sodium hydrogen carbonate (20 ml), water (2 × 20 ml), and saturated brine (20 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by flash column chromatography[10] on Merck 9385 silica gel (95 g; 3.5 cm diam. × 15.2 cm) eluting with a mixture of ethyl acetate and methanol (96:4) to give the *keto ester* (1.11 g, 65%), m.p. 90—94 °C (Found: C, 67.0; H, 6.35. $C_{20}H_{23}O_4P$ requires C, 67.0; H, 6.45%); R_F(EtOAc) 0.24; $\nu_{max.}$ 1 730 (ester), 1 710 (ketone), 1 441 (PhP), and 1 182 cm^{-1} (P=O); δ($CDCl_3$) 7.9—7.4 (10 H, m, Ph_2PO), 3.63 (3 H, s, CO_2Me), 3.56 (2 H, d, *J* 14.9 Hz, PCH_2), 2.65 [2 H, m, $C(O)CH_2$], 2.24 (2 H, m, CH_2CO_2Me), and 1.7—1.25 [4 H, $(CH_2)_2$]; *m/z* 358 (3%, M^+), 271 (39), 258 (26), 216 [19, $Ph_2P(OH)CH_2^+$], 215 [50, $Ph_2P(O)CH_2^+$], 202 (31, Ph_2POH^+), and 201 (100, Ph_2PO^+).

Methyl 7-Diphenylphosphinoyl-6-oxo-octanoate (**9c**), *by* RuO_4–$NaIO_4$ *Oxidative Cleavage.*[15]—In the same way, sodium periodiate (438 mg, 0.205 mmol), ruthenium dioxide hydrate (5 mg, 0.038 mmol), and the allylphosphine oxide (**7c**) (1.55 mg, 0.5 mmol) in carbon tetrachloride (1 ml), acetonitrile (1 ml), and water (1.5 ml) gave the keto acid as a brown gum. This was dissolved in methanol (12 ml) and an excess of diazomethane (*ca.* 0.29M solution in diethyl ether;[17] 15 ml, 4.35 mmol) was added dropwise by a flame-polished pipette with stirring at 0 °C. The solution was allowed to stand at room temperature for 1 h after which glacial acetic acid (1 drop) was added and solvent was removed by evaporation under reduced pressure. The residue was purified by flash column chromatography[10] on Merck 9385 silica gel (17 g, 1.5 cm diam. × 15.2 cm), eluting with EtOAc to give the keto ester (119 mg, 64%) with physical and spectroscopic data identical with those described below.

Methyl 7-Diphenylphosphinoyl-6-oxo-octanoate (**9c**) *by Ozonolytic Cleavage followed by Oxidative Work-up with Performic Acid.*—Following the method of Bailey,[18] ozone in oxygen (30 l h^{-1}, generated from dry oxygen by a Wallace and Tiernan Ozonator set at 250 V) was bubbled through a solution of the allylphosphine oxide (1 g, 3.2 mmol) in AnalaR methanol (100 ml) at −70 °C until a pale blue colour appeared. Residual ozone was purged with nitrogen and methanol was removed by evaporation under reduced pressure without heating. The glassy residue was dissolved in AnalaR formic acid (10 ml) and hydrogen peroxide [100 vol (28% w/v) aqueous solution; 1 ml] was added dropwise with gentle stirring at room temperature. The mixture was heated slowly to reflux over 10 min and immediately cooled to room temperature. Water (100 ml) was added and the mixture extracted with dichloromethane (4 × 30 ml). The combined organic extracts were washed with saturated aqueous sodium metabisulphite (30 ml), water (30 ml), and saturated brine (20 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was dissolved in methanol (50 ml) and an excess of diazomethane (*ca.* 0.29M in diethyl ether) added at 0 °C until the yellow colour persisted. After 10 min, glacial acetic acid was added to dispel the yellow colouration, and solvent was removed by evaporation under reduced pressure. The residue was purified by flash column chromatography[10] on Merck 9385 silica gel (95 g, 3.5 cm diam. × 15.2 cm), eluting with EtOAc to give the keto ester (0.74 g, 62%) with physical and spectroscopic data identical with those described below. A second phosphorus-containing material was eluted from the column (0.28 g of material from mixed fractions + 0.02 g pure). This more polar by-product [R_F = 0.87 × R_F of keto ester (**9c**)] was *methyl 2-diphenylphosphinoylpropanoate* (0.15 g, 15%); R_F(EtOAc) 0.33; $\nu_{max.}$($CHCl_3$) 1 730 (C=O), 1 438 (PhP), 1 180 (P=O), and 1 120 cm^{-1} (CO); δ($CDCl_3$) 8.1—7.3 (10 H, m, Ph_2PO), 3.65 (1 H, quint., *J* 7 Hz, PCH), 3.48 (3 H, s, CO_2Me), and 1.45 (3 H, dd, J_{HH} 7 and J_{PH} 16 Hz, CH*Me*) (Found: M^+, 288.0908. $C_{16}H_{17}O_3P$ requires *M*, 288.0915). This ester is a product of Baeyer-Villiger over-oxidation of the required keto acid.

6-Diphenylphosphinoyl-5-oxo-6-eicosanoic Acid (**10a**).—In the same way the allylphosphine oxide (**7a**) (5 g, 10.4 mmol) gave the *keto acid* (5.02 g, 92%), m.p. 102—104.5 °C (Found: C, 73.0; H, 9.3. $C_{32}H_{47}O_4P$ requires C, 73.0; H, 9.0%); R_F(AcOH–EtOAc, 1:99) 0.52; $\nu_{max.}$($CHBr_3$) 3 500 (OH), 1 740 (ketone), 1 705 (acid); $\nu_{max.}$(Nujol mull) 1 440 (PhP) and 1 180 (P=O); δ($CDCl_3$) 8.0—7.3 (10 H, m, Ph_2PO), 3.6 (1 H, ddd, J_{PH} 14.5, J_{HH} 3.5 and 11 Hz, PCH), 2.65 (2 H, t, $CHCOCH_2$), 2.2 (2 H, t, CH_2CO_2H), 1.75 (2 H, m, $COCH_2CH_2$), 1.8—0.7 [26 H, m, $(CH_2)_{13}$], and 0.9 (3 H, t, Me) (Found: M^+, 526.3220. $C_{32}H_{47}O_4P$ requires *M*, 526.3212); *m/z* 526 (3%, M^+), 508 (5, $M^+ - H_2O$), 258 (39), 229 (25), 219 (57, $Ph_2PO_2H_2^+$), 203 [21, $Ph_2P(OH)H^+$], 202 (100, Ph_2POH^+), and 201 (95, Ph_2PO^+).

(E)-*Methyl 7-Diphenylphosphinoyl-6-oxo-10-phenyldec-9-enoate* (**9i**).—Cinnamyl bromide (61 mg, 0.31 mmol), anhydrous potassium carbonate (100 mg, 0.72 mmol), and the keto ester (**9b**) (100 mg, 0.28 mmol) in dry distilled butan-2-one (10 ml) were heated under reflux, under nitrogen, for 17 h. The mixture was cooled, solvent was removed by evaporation under reduced pressure and the residue was purified by flash column chromatography[10] on Merck 9385 silica gel (17 g, 1.5 cm diam. × 15.2 cm), eluting with EtOAc to give the *keto ester* (80 mg, 61%), m.p. 151—155 °C (from hexane–EtOAc) (Found: C, 73.3; H, 6.7; P, 6.5. $C_{29}H_{31}O_4P$ requires C, 73.4; H, 6.6; P, 6.5%); R_F(EtOAc) 0.39; $\nu_{max.}$($CHCl_3$) 1 730 (ester) with shoulder at 1 710 (C=O), 1 440 (PhP), 1 165 (P=O), 1 120, and 970 cm^{-1} (*trans* double bond, HC=CH out-of-plane deformation); δ($CDCl_3$) 7.90—7.75 (4 H, m, Ph_2PO *ortho* protons), 7.58—7.46 (6 H, m, Ph_2PO *meta* and *para* protons), 7.28—7.15 (5 H, m, CPh), 6.33 (1 H, d, *J* 15.8 Hz, PhC*H*=CH), 5.96 (1 H, dt, *J* 15.8 and 6.9 Hz, CH=C*H*CH_2), 3.76 (1 H, dt, *J* 3.3 and 12.1 Hz, PCH), 3.59 (3 H, s, CO_2Me), 2.97 (1 H, m, $CHCH_2$*), 2.59 (1 H, m, $CHCH_2$*), 2.56 (2 H, m, $COCH_2$), 2.14 (2 H, m, CH_2CO_2Me), and 1.36 [4 H, m, $CH_2(CH_2)_2CH_2$]; *m/z* 474 (7%, M^+), 443 (3, M^+ − OMe), 331 [65, $Ph_2P(O)CHCH_2CH$=$CHPh^+$], 273 (20), 219 (30, $Ph_2PO_2H_2^+$), 203 [18, $Ph_2P(OH)H^+$], 202 (100, Ph_2POH^+), and 201 (70, Ph_2PO^+).

7-Diphenylphosphinoyl-6-oxo-octanoate (**9c**) *following the Method of Mathey and Savignac.*[19]—BuLi (1.55M solution in hexane) was added dropwise to a stirred solution of the phosphine oxide (**5**; R = Me) (8.5 g, 37 mmol) in THF (250 ml) under nitrogen at 0 °C until an orange colour persisted. Further BuLi (1.55M solution in hexane; 26 ml, 40.3 mmol) was added dropwise with stirring after which the dark red solution was cooled to −60 °C, and Aldrich 'Gold Label' copper(I) iodide (7.8 g, 41 mmol) was added in one portion. The mixture was stirred vigorously between −30 and −25 °C for 1 h to give a black suspension and was then cooled to −70 °C and methyl adipoyl chloride (6.6 h, 37 mmol) added dropwise over 5 min. Stirring was continued as the mixture was allowed, over 3 h, to warm to room temperature; it was then stirred at this temperature for 15 h. The mixture was then cooled to 0 °C, diluted with water (200 ml), and stirred at 0 °C for 5 min; the bulk of the THF was then removed by evaporation under reduced pressure. Water (100 ml) was added to the residue to give a grey suspension which was filtered through Celite; the latter was washed with EtOAc (2 × 100 ml) and the filtrates were extracted with EtOAc (3 × 100 ml). The combined organic extracts and washings were washed with water (80 ml) and saturated brine (2 × 60 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The crystalline residue was recrystallised from ethyl acetate–hexane to give the keto ester (7.58 g, 55%). The mother liquors were concentrated by

evaporation under reduced pressure to give a yellow crystalline residue. This was purified by flash column chromatography[10] on Merck 9385 silica gel (275 g; 6 cm diam. × 15.2 cm), eluting with EtOAc to give more of the *keto ester* (3.25 g, 24%) (total yield 10.83 g, 79%), m.p. 111—112 °C (Found: C, 67.7; H, 6.65; P, 8.4. $C_{21}H_{25}O_4P$ requires C, 67.7; H, 6.75; P, 8.3%); R_F(EtOAc) 0.29; $\nu_{max.}$(Nujol mull) 1 738 (ester), 1 705 (ketone), 1 440 (PhP), and 1 180 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.3 (10 H, m, Ph_2PO), 3.85—3.35 (4 H, m, PCH and CO_2Me), 2.55 (2 H, m, $COCH_2$), 2.2 (2 H, m, CH_2CO_2Me), 1.6—1.2 [4 H, m, $CH_2(CH_2)_2CH_2$], and 1.35 (3 H, dd, J_{HH} 6.5 and J_{PH} 17 Hz, $CHMe$); *m/z* 372 (40%, M^+), 341 (15, M^+ − OMe), 285 (21), 230 (55), 219 (67, $Ph_2PO_2H_2^+$), 202 (72, Ph_2POH^+), and 201 (100, Ph_2PO^+).

5-*Diphenylphosphinoyl*-4-*oxohexanoate* (**9g**).—In the same way the phosphine oxide (**5**; R = Me) (1 g, 4.3 mmol) and 3-methoxycarbonylpropionyl chloride (0.72 g, 4.8 mmol) gave the *keto ester* (0.89 g, 60%), m.p. 101—102.5 °C (Found: C, 66.3; H, 6.2; P, 8.8. $C_{19}H_{21}O_4P$ requires C, 66.3; H, 6.15; P, 9.0%); R_F(EtOAc) 0.24; $\nu_{max.}$($CHBr_3$) 1 730 (ester), 1 705 (ketone), 1 440 (PhP), and 1 180 cm^{-1} (P=O); δ($CDCl_3$) 8.0—7.3 (10 H, m, Ph_2PO), 3.9—3.4 (4 H, m, PCH and CO_2Me), 2.9 and 2.45 (2 × 2 H, AA′BB′ multiplets, $COCH_2CH_2CO_2Me$), and 1.4 (3 H, dd, J_{HH} 7 and J_{PH} 16 Hz; $CHMe$); *m/z* 344 (15%, M^+), 313 (15, M^+ − OMe), 230 (52), 229 (18), 219 (45, $Ph_2PO_2H_2^+$), 202 (53, Ph_2POH^+), and 201 (100, Ph_2PO^+).

Methyl 5-*Diphenylphosphinoyl*-4-*oxodecanoate* (**9h**).—In the same way the phosphine oxide (**5**; R = n-pentyl) (4.29 g, 15 mmol) and 3-methoxycarbonylpropionyl chloride (2.48 g, 16.5 mmol) gave the *keto ester* (4.4 g, 73%), m.p. 102.5—103.5 °C (from hexane–EtOAc) (Found: C, 68.9; H, 7.35; P, 7.5. $C_{23}H_{29}O_4P$ requires C, 69.0; H, 7.3; P, 7.7%); R_F(EtOAc–hexane, 7:3) 0.43; $\nu_{max.}$(Nujol mull) 1 740 (ester), 1 705 (ketone), 1 440 (PhP), and 1 180 cm^{-1} (P=O); δ($CDCl_3$) 8.1—7.3 (10 H, m, Ph_2PO), 3.85—3.45 (4 H, m, PCH and CO_2Me), 2.9 and 2.45 (2 × 2 H, AA′BB′ multiplets, $COCH_2CH_2CO_2Me$), 1.6—1.0 [8 H, m, $(CH_2)_4$], and 0.85 (3 H, distorted t, CH_2Me); *m/z* 400 (10%, M^+), 369 (13, M^+ − OMe), 330 (53), 242 (48), 229 (45), 219 (37, $Ph_2PO_2H_2^+$), 202 (83, Ph_2POH^+), and 201 (100, Ph_2PO^+).

5-*Diphenylphosphinoyl*-4-*oxohexanoic Acid* (**10g**).—BuLi (1.55M solution in hexane) was added dropwise to the phosphine oxide (**5**; R = Me) (1.15 g, 5 mmol) in THF (100 ml) at 0 °C under nitrogen until the pale orange colour persisted. Further BuLi (1.55M solution; 3.25 ml, 5 mmol) was added dropwise after which the red solution was cooled to −70 °C, and a solution of succinic anhydride (0.5 g, 5 mmol) in THF (20 ml) was added. After 10 min, the solution was allowed to warm to room temperature and saturated aqueous ammonium chloride (50 ml) was added. The mixture was acidified to pH *ca.* 3 with dilute HCl after which the bulk of the THF was removed by evaporation under reduced pressure; dilute HCl (10 drops) was then added, and the mixture extracted with dichloromethane (3 × 30 ml). The combined organic extracts were washed with water (35 ml) and saturated brine (30 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The gum was purified by dissolution in dichloromethane (100 ml) and extraction with water and sodium hydrogen carbonate (to pH 7—8) (3 × 30 ml). The organic phase was dried ($MgSO_4$) and evaporated under reduced pressure to give recovery of phosphine oxide (**5**; R = Me) (0.68 g, 59%). The combined aqueous extracts were acidified to pH 1 by dilute hydrochloric acid and the mixture was extracted with dichloromethane (3 × 30 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. A portion (300 mg) of the residue (0.86 g) was further purified by preparative layer chromatography, eluting with a mixture of methanol, acetic acid, and EtOAc (2:5:93) to give the *keto acid* (210 mg, 36%) as a colourless semi-crystalline solid, R_F(MeOH–AcOH–EtOAc, 2:5:93) 0.38; $\nu_{max.}$($CDCl_3$) 3 700—2 300 (OH), 1 712 (C=O), and 1 442 cm^{-1} (PhP); δ($CDCl_3$) 10.0 (1 H, br s, CO_2H), 8.1—7.2 (10 H, m, Ph_2PO), 3.8 (1 H, dq, J_{PH} 15 and J_{HH} 7.5 Hz, PCH), 2.8 (2 H, t, *J* 7 Hz, $COCH_2$), 2.4 (2 H, t, *J* 7 Hz, CH_2CO_2Me), and 1.35 (3 H, dd, J_{HH} 7 and J_{PH} 16.5 Hz, $CHMe$) (Found: M^+, 330.1019. $C_{18}H_{19}O_4P$ requires 330.1021); *m/z* 330 (3%, M^+), 219 (32, $Ph_2PO_2H_2^+$), 202 (71, Ph_2POH^+), and 201 (100, Ph_2PO^+).

7-(1-*Diphenylphosphinoylethyl*)*oxepan*-2-*one* (**12c**).—Water (15 ml) and lithium hydroxide monohydrate (400 mg, 9.5 mmol) were added to a solution of the keto ester (**9c**) (1 g, 2.7 mmol) in THF (15 ml) and the mixture was stirred vigorously at room temperature under nitrogen for 15 h. Dilute hydrochloric acid was added at 0 °C to acidify the mixture to pH 1 after which the bulk of the THF was removed by evaporation under reduced pressure and the mixture extracted with EtOAc (3 × 30 ml). The combined organic extracts were washed with saturated brine (20 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give the crude 7-diphenylphosphinoyl-6-oxo-octanoic acid (**11c**) as a colourless gum (1.02 g). This was dissolved in acid-free distilled ethanol (50 ml) and sodium borohydride (110 mg, 2.9 mmol) was added gradually with stirring at 0 °C. Stirring was continued at 0 °C for 5 min, until effervescence had subsided, and then at room temperature for 10 min. Further sodium borohydride (110 mg, 2.9 mmol) was added gradually, and stirring was continued at room temperature for 2 h. The solution was cooled to 0 °C, after which saturated aqueous ammonium chloride (15 ml) was added gradually and the mixture acidified to pH 1 by dilute HCl. The bulk of the ethanol was removed by evaporation under reduced pressure after which the mixture was diluted with water (30 ml) and extracted with EtOAc (3 × 30 ml). The combined organic extracts were washed with dilute HCl (20 ml) and saturated brine (20 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give a crude mixture of 7-diphenylphosphinoyl-6-hydroxyoctanoic acid diastereoisomers as a colourless foam (0.99 g). Dry toluene (100 ml) and toluene-*p*-sulphonic acid monohydrate (*ca.* 30 mg, *ca.* 0.16 mmol) were added and the mixture was heated under reflux under nitrogen with azeotropic removal of water for 4 h. The solution was cooled, toluene was removed by evaporation under reduced pressure, and the residue was extracted with EtOAc (3 × 40 ml). The combined extracts were washed with dilute aqueous sodium hydrogen carbonate (*ca.* 1% w/w solution; 30 ml), water (30 ml), and saturated brine (25 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give a white foam which was shown (n.m.r.) to be a 77:23 *threo*:*erythro* mixture. This was purified by flash column chromatography[10] on Merck 9385 silica gel (50 g; 2.5 cm diam. × 15.2 cm), eluting with EtOAC (300 ml), methanol–EtOAc (3:97; 300 ml), and methanol–EtOAc (5:95) to give the [*RS*-(*R**,*R**)] diastereoisomer, *lactone threo*-(**12c**) (0.58 g, 63%), m.p. 185—186 °C (Found: C, 69.95; H, 6.7; P, 9.3. $C_{20}H_{23}O_3P$ requires C, 70.15; H, 6.75; P, 9.1%); R_F(EtOAc) 0.18; $\nu_{max.}$($CHCl_3$) 1 720 (C=O), 1 440 (PhP), 1 295 (CO), 1 180 (P=O), and 1 160 cm^{-1} (CO); δ($CDCl_3$) 8.0—7.3 (10 H, m, Ph_2PO), 4.43 (1 H, ddd, *J* 9.0, 6.24, and J_{HH} *threo*-vicinal 2.5 Hz, OCH), 2.90 (1 H, dqd, J_{HH} *threo*-vicinal 2.5, J_{HMe} 7.2, and J_{PH} 9.8 Hz, PCH), 2.8—1.0 [8 H, m, $(CH_2)_4$], and 1.26 (3 H, dd, J_{HH} 7.2 and J_{PH} 16.0 Hz, Me); *m/z* 342 (8%, M^+), 219 (100, $Ph_2PO_2H_2^+$), 202 (98, Ph_2POH^+), and 201 (66, Ph_2PO^+). The second product to elute from the column was the [RS-(*R**,*S**)] diastereoisomer, *lactone erythro*-(**12c**) (0.17 g, 19%), m.p. 147—149.5 °C (Found: C, 70.0; H, 6.8; P, 8.85. $C_{20}H_{23}O_3P$ requires C,

70.2; H, 6.75; P, 9.05%); R_F(EtOAc) 0.1; $\nu_{max.}$($CHCl_3$) 1 730 (C=O), 1 440 (PhP), 1 290 (CO), and 1 180 (P=P) with a shoulder at 1 160 cm^{-1} (CO); δ($CDCl_3$) 8.0—7.3 (10 H, m, Ph_2PO), 5.03—4.68 (1 H, m, OCH), 2.95—2.35 (3 H, m, PCH and $COCH_2$), 2.2—1.1 [6 H, $OCH(CH_2)_3$], and 1.26 (3 H, dd, J_{HH} 7.3 and J_{PH} 16.8 Hz, Me); *m/z* 342 (2%, M^+), 219 (57, $Ph_2PO_2H_2^+$), 202 (100, Ph_2POH^+), and 201 (59, Ph_2PO^+).

5-(1-*Diphenylphosphinoylhexyl*)*tetrahydrofuran*-2-*one* (**12h**).—Sodium borohydride (100 mg, 2.6 mmol) was added to a stirred solution of the keto ester (**9h**) (1.5 g, 3.75 mmol) in methanol at 0 °C. Stirring was continued at room temperature for 80 min with two further additions of sodium borohydride (40 mg, 1 mmol) and (70 mg, 1.8 mmol) after 40 min and 1 h, respectively. The mixture was cooled to 0 °C, saturated aqueous ammonium chloride (20 ml) was added, and the mixture was extracted with EtOAc (3 × 25 ml). The combined organic extracts were washed with saturated brine (20 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give a colourless gum (1.5 g). A solution of this gum in trifluoroacetic acid (20 ml) was stirred at room temperature under nitrogen for 1.25 h after which trifluoroacetic acid was removed by evaporation under reduced pressure and the residue dissolved in ethyl acetate (100 ml). The solution was washed with 8% aqueous sodium hydrogen carbonate (50 ml), water (30 ml), and saturated brine (20 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by flash column chromatography[10] on Merck 9385 silica gel (130 g; 4 cm diam. × 15.2 cm), eluting with EtOAc to give the *lactone* (1.17 g, 84%) as a mixture of the *erythro* [*RS*-(*R**,*S**)] and *threo* [*RS*-(*R**,*R**)] diastereoisomers, in the ratio 43:57 (h.p.l.c.). These diastereoisomers were separated by preparative h.p.l.c. (Zorbax Silica 25 cm × 2.1 cm i.d., *ca.* 20 mg sample per injection, eluting with hexane–ethanol (94:6) at 10 ml min^{-1}, u.v. detection at 220 nm). The first product to be eluted was the *RS*-(*R**,*R**)] diastereoisomer, *lactone threo*-(**12h**), m.p. 142.5—144 °C (Found: C, 71.6; H, 7.2. $C_{22}H_{27}O_3P$ requires C, 71.3; H, 7.35%); R_F(EtOAc) 0.30; h.p.l.c. R_T(hexane–EtOH, 9:1 as above) 12.02 min; $\nu_{max.}$($CHCl_3$) 1 775 (C=O), 1 440 (PhP), and 1 180 cm^{-1} (P=O); δ($CDCl_3$) 7.95—7.75 (4 H, m, Ph_2PO *ortho* protons), 7.65—7.45 (6 H, m, Ph_2PO *meta* and *para* protons), 4.80—4.69 (1 H, m, OCH), 2.93 (1 H, dtd, J_{HH} *threo* 3.8, J_{HH} *vicinal* methylene 5.6, and J_{PH} 10.0 Hz, PCH), 2.6—2.2 (4 H, m, $COCH_2CH_2$), 1.9—1.5 (2 H, m, $PCHCH_2$), 1.35—0.95 [6 H, m, $(CH_2)_3$Me], and 0.73 (3 H, t, *J* 6.6 Hz, Me) (Found: M^+, 370.1684. $C_{22}H_{27}O_3P$ requires *M*, 370.1698); *m/z* 370 (14%, M^+), 219 (55, $Ph_2PO_2H_2^+$), 202 (100, Ph_2POH^+), and 201 (44, Ph_2PO^+). The second product to be eluted was the [*RS*-(*R**,*S**)] diastereoisomer, *lactone erythro*-(**12h**), m.p. 127—130 °C; R_F(EtOAc) 0.30; h.p.l.c. R_T(hexane–EtOH, 9:1) 13.25 min; $\nu_{max.}$($CHCl_3$) 1 775 (C=O), 1 440 (PhP), and 1 180 cm^{-1} (P=O); δ($CDCl_3$) 7.9—7.75 (4 H, m, Ph_2PO *ortho* protons), 7.6—7.45 (6 H, m, Ph_2PO *meta* and *para* protons), 4.86 (1 H, tdd, J_{HH} *vicinal* methylene 7.1, J_{HH} *erythro* 8.1, J_{PH} 11.6 Hz, OCH), 2.75—2.60 (1 H, m, PCH), 2.43 and 2.13 (2 H and 2 H, AA′BB′ multiplets, $COCH_2CH_2$), 1.9—0.95 [8 H, m, $(CH_2)_4$], and 0.75 (3 H, t, *J* 6.8 Hz, Me) (Found: M^+, 370.1706. $C_{22}H_{27}O_3P$ requires *M*, 370.1698); *m/z* 370 (72%, M^+), 219 (45, $Ph_2PO_2H_2^+$), 202 (100, Ph_2POH^+), and 201 (47, Ph_2PO^+).

6-(1-*Diphenylphosphinoylpentadecyl*)*tetrahydro*-2H-*pyran*-2-*one* (**12a**), via *Lactonisation with TFAA*.—Sodium borohydride (150 mg, 4 mmol) was added gradually to a stirred solution of the keto acid (**10a**) (0.97 g, 1.8 mmol) in ethanol (30 ml) at 0 °C. Further sodium borohydride (75 mg, 2 mmol) was added as effervescence subsided and the mixture was stirred at room temperature for 1 h. Saturated aqueous ammonium chloride (50 ml) was added and the bulk of the ethanol was evaporated under reduced pressure. The residue was diluted with water (50 ml) and the mixture acidified to pH 1 with dilute HCl and extracted with EtOAc (3 × 30 ml). The combined organic extracts were washed with water (30 ml) and saturated brine (20 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give an off-white solid residue which was dissolved in dry AnalaR benzene (200 ml). Trifluoroacetic anhydride (0.52 g, 2.5 mmol) was then added dropwise to the stirred solution at 7 °C, under nitrogen. Stirring was continued at 7 °C for 24 h after which the mixture was diluted with water (50 ml) and separated. The organic phase was washed with saturated aqueous sodium hydrogen carbonate (50 ml), water (50 ml), and saturated brine (30 ml), dried ($MgSO_4$), and evaporated under reduced pressure to give a pale brown oil. This was purified by flash column chromatography[10] on Merck 9385 silica gel (95 g, 3.7 cm diam. × 15.2 cm), eluting with EtOAc, to give the [*RS*-(*R**,*R**)] diastereoisomer, *lactone threo*-(**12a**) (0.47 g, 51%), m.p. 94—95 °C (from diethyl ether–hexane) (Found: C, 75.1; H, 9.35; P, 5.9. $C_{32}H_{47}O_3P$ requires C, 75.3; H, 9.3; P, 6.1%); R_F(EtOAc) 0.29; $\nu_{max.}$($CHBr_3$) 1 715 (C=O) and 1 438 cm^{-1} (PhP); δ($CDCl_3$) 7.9—7.75 (4 H, m, Ph_2PO *ortho* protons), 7.6—7.4 (6 H, m, Ph_2PO *meta* and *para* protons), 4.52 [1 H, dddd (elucidated by decoupling), J_{HH} *threo* 2.6, J_{HH} *vicinal* methylene protons 3 and 7, and J_{PH} 11.5 Hz, OCH], 2.83 [1 H, dddd (elucidated by decoupling), J_{HH} *threo* 2.6, J_{HH} *vicinal* methylene protons 4.8 and 5.6, and J_{PH} 13 Hz, PCH], 2.6—2.2 [3 H, m, $COCH_2$ and $OCHC(H)H^*CH_2$], 1.94—1.54 [5 H, m, $C(O)CH_2CH_2C(H^*)HCHO$ and $PCHCH_2$], 1.4—0.9 [24 H, m, $(CH_2)_{12}$Me], and 0.84 (3 H, t, *J* 3 Hz, Me); *m/z* 510 (12%, M^+), 466 (8, $M^+ - CO_2$), 219 (34, $Ph_2PO_2H_2^+$), 203 [31, $Ph_2P(OH)H^+$], 202 (100, Ph_2POH^+), and 201 (48, Ph_2PO^+). The second product to be eluted was the [*RS*-(*R**,*S**)] diastereoisomer, *lactone erythro*-(**12a**) (70 mg, 8%), m.p. 119—122 °C (from diethyl ether–hexane), R_F(EtOAc) 0.21; $\nu_{max.}$($CHBr_3$) 1 725 (C=O) and 1 438 cm^{-1} (PhP); δ($CDCl_3$) 7.9—7.8 (4 H, m, Ph_2PO *ortho* protons), 7.5—7.4 (6 H, m, Ph_2PO *meta* and *para* protons), 4.67 [1 H, dddd (elucidated by decoupling), J_{HH} *erythro* 4, J_{HH} *vicinal* methylene protons 3 and 11, J_{PH} 17 Hz, OCH], 2.69 [1 H, tt (elucidated by decoupling), J_{HH} *erythro* 4, J_{HH} *vicinal* methylene protons 4 and 8, and J_{PH} 8 Hz, PCH], 2.41 [1 H, dm, J_{HH} *geminal* 17.6 Hz, $OCHC(H)H^*CH_2$], 2.11—2.00 (2 H, m, $COCH_2$), 1.96—1.51 [5 H, m, $COCH_2CH_2C(H^*)HCH{\cdot}O$ and $PCHCH_2$], 1.5—0.9 [24 H, m, $(CH_2)_{12}$Me], and 0.87 (3 H, t, *J* 6.6 Hz, Me) (Found: M^+, 510.3256. $C_{32}H_{47}O_3P$ requires *M*, 510.3263); *m/z* 510 (7%, M^+), 466 (10, $M^+ - CO_2$), 219 (34, $Ph_2PO_2H_2^+$), 203 [28, $Ph_2P(OH)H^+$], 202 (100, Ph_2POH^+), and 201 (44, Ph_2PO^+).

Methyl [RS-(R*,S*)]-6-*Hydroxy*-7-*diphenylphosphinoyloctanoate* (**14**).—Potassium carbonate (200 mg, 1.5 mmol) was added to a solution of the lactone *erythro*-(**12c**) (100 mg, 0.3 mmol) in dry methanol (1 ml) and the mixture stirred at room temperature for 3 h. Water (20 ml) was added and the mixture was extracted with ethyl acetate (3 × 10 ml) The combined organic extracts were washed with saturated brine (8 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give the *hydroxy ester* (86 mg, 77%), R_F(EtOAc) 0.26; δ($CDCl_3$) 7.95—7.7 (4 H, m, Ph_2PO *ortho* protons), 7.6—7.45 (6 H, m, Ph_2PO *meta* and *para* protons), 4.28 (1 H, s, OH), 4.18—3.95 (1 H, m, CHOH), 3.66 (3 H, s, CO_2Me), 2.39 (1 H, quint., *J* 6 Hz, PCH), 2.29 (2 H, t, *J* 7.5 Hz, $CH_2CO_2CH_3$), 1.8—1.2 [6 H, m, $CH(CH_2)_3$], and 1.18 (3 H, dd, J_{HH} 7.5 and J_{PH} 18 Hz, CH*Me*) (Found: M^+, 374.1675. $C_{21}H_{27}O_4P$ requires *M*, 374.1647); *m/z* 375 (8%, M^+), 374 (7, $M^+ - H$), 259 (52), 230 [100, $Ph_2P(OH)CHCH_3^+$], 229 [26, $Ph_2P(O)CHMe^+$], 202 [58, Ph_2POH^+], and 201 [61, Ph_2PO^+].

Synthesis of Unsaturated Acids (*see Footnotes to Table* 6).—(E)-*Oct*-6-*enoic acid*, *E*-(**1c**). Potassium hydroxide [86.5% (w/w) pellets, assayed by titration against 0.1M HCl; 2.8 g, 43 mmol] was dissolved in water to give 40 ml of 6.06% (w/v) aqueous potassium hydroxide. Of this solution, 10 ml (10.8 mmol of KOH) were added dropwise to a stirred solution of the lactone *threo*-(**12c**) (1 g, 2.9 mmol) in THF (15 ml). Water (5 ml) was then added and the mixture stirred at room temperature for 20 h. After this solvent was removed by freeze-drying, dry DMSO (100 ml) was added, and the mixture was stirred at 50 °C under nitrogen for 1 h. The solution was cooled and water (150 ml) added slowly to it; it was then cooled to 0 °C, brought to pH 1 with 5% HCl, and extracted at 0 °C with freshly distilled diethyl ether (4 × 50 ml). The combined organic extracts were washed with 1% HCl (30 ml) and saturated brine (30 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The white residue, which consisted of the required unsaturated acid and diphenylphosphinic acid, was purified by flash column chromatography[10] on Merck 9385 silica gel (50 g, 2.5 cm diam. × 15.2 cm), eluting with a mixture of light petroleum (b.p. 40—60 °C) and freshly distilled diethyl ether (1:1), to give a colourless oil (400 mg). This oil (390 mg) was further purified by bulb-to-bulb distillation at 0.4 mmHg (Kugelrohr oven temperature 80 °C) to give the unsaturated acid (373 mg, 93%) as a colourless oil, b.p. *ca.* 80 °C/0.4 mmHg (lit.,[20] 90 °C/1.2 mmHg); R_F(eluant as above) 0.64 (alkaline $KMnO_4$ spray detection); $\nu_{max.}$(film) 2 945 br (OH), 1 705 (C=O), and 975 cm^{-1} (vinylic CH); δ($CDCl_3$) 5.48—5.38 (2 H, m, HC=CH), 2.33 (2 H, t, *J* 5.9 Hz, CH_2CO_2H), 2.03—1.95 (2 H, m, C=CHCH_2), 1.68—1.56 [5 H, m, Me and C=CCH_2CH_2], and 1.45—1.32 (2 H, m, $CH_2CH_2CO_2H$), J_{HH} vicinal (vinylic protons across *trans* double bond) 15.2 Hz from 400 MHz spectrum with decoupling of vinylic methyl group at δ 1.62 (Found: M^+, 142.0983. $C_8H_{14}O_2$ requires *M*, 142.0994); *m/z* 142 (7%, M^+), 124 (34, $M^+ - H_2O$), 96 (30, $M^+ - CO_2H_2$), 82 (45), 67 (71), and 55 (100, $CH_3CH{=}CHCH_2^+$). None of the *Z*-isomer was detected by g.l.c.

(Z)-*Oct*-6-*enoic acid*, *Z*-(**1c**). In the same way the lactone *erythro*-(**12c**) (0.17 g, 0.5 mmol) gave the unsaturated acid (64 mg, 91%) as a colourless oil, b.p. *ca.* 55 °C/0.2 mmHg, (Kugelrohr bulb-to-bulb distillation) (lit.,[20] 88 °C/0.8 mmHg), R_F[light petroleum (b.p. 40—60 °C)–Et_2O, 1:1] 0.39 (alkaline $KMnO_4$ spray detection); $\nu_{max.}$ 2 945br (OH), 1 705 (C=O), and 720 cm^{-1} (vinylic CH); δ($CDCl_3$) 5.5—5.30 (2 H, m, HC=CH) [irradiation of the allylic methyl group simplifies these signals to 5.42 (1 H, d, J_{cis} 10.87 Hz, MeC*H*) and 5.35 (1 H, dt, *J* 10.87 and 6.55 Hz, C=C*H*CH_2)], 2.35 (2 H, t, *J* 7.4 Hz, CH_2CO_2H), 2.06 (2 H, q, *J* 7.2 Hz, C=CHCH_2), 1.71—1.58 (5 H, m, Me and C=CHCH_2), and 1.46—1.34 (2 H, m, $CH_2CH_2CO_2H$) (Found: 142.0994. $C_8H_{14}O_2$ requires *M*, 142.0994); *m/z* 142 (8%, M^+), 124 (34, $M^+ - H_2O$), 96 (29, $M^+ - CO_2H_2$), 82 (63), 67 (50), and 55 (100, $CH_3CH{=}CHCH_2^+$). The product contained 0.1% of the *E*-isomer by g.l.c.

Samples of both the *E* and *Z* unsaturated acids prepared as above, were methylated by dropwise addition of diazomethane in diethyl ether[17] to allow geometrical isomer separation of the methyl esters to capillary column g.l.c. (Mega SE54 15m silica, oven temperature 70 °C, 1.5 ml min^{-1} hydrogen carrier gas).

(E)-*Eicos*-5-*enoic acid*, *E*-(**1a**). In the same way, the lactone *threo*-(**12a**) (0.8 g, 1.57 mmol) gave the acid (0.43 g, 88%) as a white waxy solid, m.p. 52.5—54 °C (Found: C, 77.3; H, 12.6. $C_{20}H_{38}O_2$ requires C, 77.4; H, 12.35%); R_F(Et_2O) 0.67 (alkaline $KMnO_4$ spray detection); $\nu_{max.}$($CHCl_3$) 3 000br (OH), 1 720 (C=O), and 980 cm^{-1} (vinylic CH); δ($CDCl_3$) 5.43 (1 H, dt, J_{trans} 15.0 and *J* 5.5 Hz, vinylic H), 5.33 (1 H, dt, J_{trans} 15.0 and *J* 5.5 Hz, vinylic H), 2.34 (2 H, t, *J* 7.5 Hz, CH_2CO_2H), 2.03 (2 H, q, *J* 6.8 Hz, allylic CH_2), 1.96 (2 H, q, *J* 6.0 Hz, allylic CH_2), 1.69 (2 H, quint., *J* 7.2 Hz, $CH_2CH_2CO_2H$], 1.36—1.20 [24 H, m, $(CH_2)_{12}$Me], and 0.87 (3 H, t, *J* 6.6 Hz, Me); *m/z* 310 (6%, M^+), 292 (13, $M^+ - H_2O$), 97 [49, HC=CH$(CH_2)_3COH^+$], 83 [52, $CH(CH_2)_3CO^+$], 81 (46), 69 (61, $C_5H_9^+$), 67 (55), 57 (78, $C_4H_9^+$), and 55 (100, $C_4H_7^+$). None of the *Z*-isomer was detected by capillary column g.l.c. (on Mega SE54 15 m, oven temperature 300 °C, 1.5 ml min^{-1} hydrogen carrier gas).

(Z)-*Eicos*-5-*enoic acid*, *Z*-(**1a**). In the same way, the lactone *erythro*-(**12a**) (0.14 g, 0.275 mmol) gave the acid (47 mg, 55%) as a white waxy solid, m.p. 24—27 °C (lit.,[21] 26—27 °C); R_F(Et_2O) 0.67 (alkaline $KMnO_4$ spray detection); $\nu_{max.}$($CHCl_3$) 3 050br (OH) and 1 705 cm^{-1} (C=O); δ($CDCl_3$) 5.48—5.25 (2 H, m, J_{cis} 10.8 Hz, HC=CH), 2.35 (2 H, t, *J* 7.5 Hz, CH_2CO_2H), 2.09 (2 H, q, *J* 7.2 Hz, allylic CH_2), 2.00 (2 H, q, *J* 6.7 Hz, allylic CH_2), 1.69 (2 H, quint., *J* 7.3 Hz, $CH_2CH_2CO_2H$), 1.4—1.2 [24 H, m, $(CH_2)_{12}$Me], and 0.87 (3 H, t, *J* 6.6 Hz, Me) (Found: M^+, 310.2884. $C_{20}H_{38}O_2$ requires *M*, 310.2872); *m/z* 310 (2%, M^+), 292 (26, $M^+ - H_2O$), 97 [37, HC=CH$(CH_2)_3COH^+$], 83 [36, $CH(CH_2)_3CO^+$], 81 (37), 69 (52, $C_5H_9^+$), 67 (49), 57 (72, $C_4H_9^+$), and 55 (100, $C_4H_7^+$). The product contained 0.1% of the *E*-isomer, detected by capillary column g.l.c.

(E)-*Dec*-4-*enoic acid*, *E*-(**1h**). In the same way the lactone *threo*-(**12h**) (300 mg, 0.81 mmol) gave the unsaturated acid (101 mg, 73%) as a colourless oil, m.p. 4—5 °C; R_F(Et_2O) 0.65 ($KMnO_4$ spray detection); $\nu_{max.}$(film) 3 040 (OH), 1 710 (C=O), and 985 cm^{-1} (vinylic CH); δ($CDCl_3$) 5.47 (1 H, dtt, J_{trans} 15.4, $J_{vicinal}$ 6.4, and $J_{allylic}$ 1 Hz, vinylic H), 5.39 (1 H, dtt, J_{trans} 15.4, $J_{vicinal}$ 6.2, and $J_{allylic}$ 1 Hz, vinylic H), 2.41 and 2.30 (2 H, and 2 H, AA′BB′ multiplets, $HO_2CCH_2CH_2$), 1.96 [2 H, q, *J* 7.0 Hz, $CH_2(CH_2)_3Me$], 1.36—1.20 [6 H, m, $(CH_2)_3$Me], and 0.87 (3 H, t, *J* 7.0 Hz, Me) (Found: M^+, 170.1300. $C_{10}H_{18}O_2$ requires *M*, 170.1307); *m/z* 170 (12%, M^+), 152 (20, $M^+ - H_2O$), 110 (43, pentCH:$CHCH^+$), 84 (34, pentCH^+), 81 (47), 69 (91, $C_5H_9^+$), 68 (55), 60 [26, $H_2C(OH)_2^+$], and 55 (100, $C_4H_7^+$). Addition of diazomethane in ether to the crude product and capillary column g.l.c. (15 m Carbowax 20M with hydrogen carrier gas at 1.5 ml min^{-1} and oven temperature 70 °C) showed 0.5% of the *Z-isomer.*

(Z)-*Dec*-4-*enoic acid*, *Z*-(**1h**) *by freeze-drying.* 2.87% (w/v) Aqueous potassium hydroxide solution (1 ml; 0.51 mmol of KOH), the lactone *erythro*-(**12h**) (80 mg, 0.22 mmol), and distilled THF (1 ml) were stirred at room temperature for 16 h after which solvent was removed by evaporation under reduced pressure and freeze-drying. The residue was stirred with dry DMSO (10 ml) at 50 °C for 1 h after which the mixture was cooled, diluted with water (20 ml), and brought to pH 1 with dilute HCl; the cooled solution was then extracted with diethyl ether (4 × 10 ml). The combined organic extracts were washed with 1% HCl (8 ml) and saturated brine (6 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by flash column chromatography[10] on Merck 9385 silica gel (10 g, 1.1 cm diam. × 15.2 cm), eluting with diethyl ether, to give the unsaturated acid (20 mg, 55%) as a colourless oil, R_F(Et_2O) 0.65 ($KMnO_4$ spray detection); $\nu_{max.}$($CHCl_3$) 3 050br (OH), 1 700 (C=O), and 920 cm^{-1} (vinylic CH); δ($CDCl_3$) (400 MHz) 5.43 (1 H, dtt, J_{cis} 10.8, $J_{vicinal}$ 7.2, and $J_{allylic}$ 1.2 Hz, pentCH=C), 5.32 [1 H, dtt, J_{cis} 10.8, $J_{vicinal}$ 6.95, and $J_{allylic}$ 1.3 Hz, C=C*H*$(CH_2)_2CO_2H$], 2.42—2.33 (4 H, m, $CH_2CH_2CO_2H$), 2.03 (2 H, dq, $J_{allylic}$ 1.2 and $J_{geminal}$ 7.2 Hz, BuCH_2CH), 1.37—1.23 [6 H, m, $(CH_2)_3$Me], and 0.87 (3 H, t, *J* 6.9 Hz, Me) (Found: M^+, 170.1310. $C_{10}H_{18}O_2$ requires *M*, 170.1307); *m/z* 170 (5%, M^+), 152 (18, $M^+ - H_2O$), 110 (34, pentCH:$CHCH^+$), 84 (32, pentCH^+), 81 (50), 71 (35), 69 (55, $C_5H_9^+$), 68 (56), 67 (55), 60 [28, $H_2C(OH)_2^+$], and 55 (100, $C_4H_7^+$). Addition of diazomethane in ether to the product and capillary column g.l.c. (15 m Carbowax 20M, hydrogen carrier gas at 1.5 ml min^{-1}, oven at 70 °C) showed 3% of the *E*-isomer.

Elimination of Diphenylphosphinic Acid from Lactone erythro-(**12h**) *Using Sodium Hydride after Lactone Hydrolysis and Freeze-drying.*—Sodium hydroxide (150 mg, 3.75 mmol) was added to a solution of the lactone *erythro*-(**12h**) (300 mg, 0.81 mmol) in distilled THF (5 ml) and water (5 ml). The mixture was stirred at room temperature under nitrogen for 24 h and solvent removed by freeze-drying. Dry DMF (5 ml) was added followed by a suspension of sodium hydride [150 mg, prewashed with hexane (2 × 5 ml)] in dry DMF (10 ml) and the mixture was stirred at 60 °C under nitrogen for 1 h. It was then cooled to room temperature, diluted with water (60 ml), and brought to pH 3 with dilute HCl to pH 3; the cooled solution was then extracted with diethyl ether (4 × 25 ml). The combined organic extracts were washed with 1% HCl (25 ml) and saturated brine (20 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by flash column chromatography [10] on Merck 9385 silica gel (12 g, 1.3 cm diam. × 15.2 cm), eluting with diethyl ether–hexane (3:2). Bulb-to-bulb distillation by Kugelrohr gave a mixture of (*Z*)-dec-4-enoic and (*E*)-dec-4-enoic acids in the ratio *ca.* 2:1 (^{13}C n.m.r., sp^2 peak integrals).

Acknowledgements

We thank S.E.R.C. and Glaxo Group Research (Ware) for a CASE award and Dr. Eric Collington for many helpful discussions.

References

1 L. D. Bergelson and M. M. Shemyakin, *Angew. Chem., Int. Ed. Engl.*, 1964, **3**, 250; I. Gosney and A. G. Rowley in 'Organophosphorus Reagents in Organic Synthesis,' ed. J. I. G. Cadogan, Academic Press, London, 1979, pp. 17—154.
2 J. S. Bindra and R. Bindra, 'Prostaglandin Synthesis,' Academic Press, New York, 1977.
3 D. Denney and L. Smith, *J. Org. Chem.*, 1962, **27**, 3404.
4 B. E. Maryanoff, A. R. Reitz, and B. A. Duhl-Emswiler, *J. Am. Chem. Soc.*, 1985, **107**, 217.
5 Preliminary communication: D. Levin and S. Warren, *Tetrahedron Lett.*, 1985, **26**, 505.
6 A. D. Buss and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2307.
7 A. H. Davidson and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1979, 639; R. S. Torr and S. Warren, *ibid.*, 1983, 1169; A. Bell, A. H. Davidson, C. Earnshaw, H. K. Norrish, R. S. Torr, D. B. Trowbridge, and S. Warren, *ibid.*, 2879.
8 A. H. Davidson, C. Earnshaw, J. I. Grayson, and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1452.
9 A. D. Buss, N. Greeves, D. Levin, P. Wallace, and S. Warren, *Tetrahedron Lett.*, 1984, **25**, 357.
10 W. C. Still, M. Kahn, and A. Mittra, *J. Org. Chem.*, 1978, **43**, 2923.
11 T. Mukaiyama, M. Usui, and K. Saigo, *Chem. Lett.*, 1976, 49.
12 A. D. Buss, W. B. Cruse, O. Kennard, and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1984, 243.
13 D. Levin and S. Warren, *Tetrahedron Lett.*, 1986, **27**, 2265.
14 A. H. Davidson, I. Fleming, J. I. Grayson, A. Pearce, R. L. Snowden, and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1977, 550.
15 P. H. J. Carlsen, T. Katsuki, V. S. Martin, and K. B. Sharpless, *J. Org. Chem.*, 1981, **46**, 3936.
16 L. F. Fieser and M. Fieser, 'Reagents for Organic Synthesis,' Wiley, New York, 1967, Vol. 1, p. 11, 'acetyl chloride.'
17 H. B. Hopps, *Aldrichimica Acta*, 1970, **3**, 9, 13; T. H. Black, *ibid.*, 1983, **16**, 1.
18 P. S. Bailey, *J. Org. Chem.*, 1957, **22**, 1548.
19 F. Mathey and P. Savignac, *Synthesis*, 1976, 766; *Tetrahedron*, 1978, **34**, 649.
20 J. H. Knight and J. H. Diamond, *J. Org. Chem.*, 1959, **24**, 400.
21 C. R. Smith, M. O. Bagby, T. K. Miwa, R. L. Lohmar, and I. A. Wolff, *J. Org. Chem.*, 1960, **25**, 1770.

Received 7th August 1987; *Paper* 7/1464