Tetrahedron Vol 37, No 23, pp. 3911 to 3920, 1981
Printed in Great Britain

0040-4020/81/233911-10$02.00/0
Pergamon Press Ltd

STEREOCONTROLLED SYNTHESIS OF CONJUGATED POLYENE ISOPRENOIDS USING PHOSPHINE OXIDE ANION INTERMEDIATES

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(*Received in U.S.A. 5 May* 1981)

Abstract—The potential for the Horner–Wittig reaction in the stereocontrolled synthesis of conjugated polyene isoprenoids is investigated. It is shown that metallations of the *Z*- and *E*-phosphine oxides (**4** and **5**), followed by reaction with *Z*- and *E*- citrals lead , in single steps, to the corresponding isomeric pentaenes (**6**) showing complete preservaation of the *Z*- and *E*-geometries in the starting materials. Although the single step reactions leading to **6** proceed in low overall yields (10–20%), the olefinations occur with >98% *E*-stereoselectivity. Isolation of the intermediate β-hydroxyphosphine oxides (e.g. **14**), followed by subsequent treatment with sodium hydride in dimethylformamide, demonstrate that these features of the reaction are associated largely with the remarkably slow rates of elimination from the *erythro*-intermediates in comparison with the *threo*-intermediates.

Condensation between **4** and the ester-aldehyde (**20**) leads to the *Z*-**6** ester **21** (34%). After conversion of **21** into the tetraenal (**25**), reaction with the phosphine oxide (**26**), followed by separation of the *erythro*-β-hydroxyphosphine oxide intermediate **27** and treatment with NaH in DMF, leads to the di-*Z*-octaene (**28**). The octaene **28** shows closely similar spectral data to those found in natural di-*Z*-phytofluene (**2**) isolated from fruit of the Tangerine tomato, *Lycopersicon esculentum* var. In a similar manner, reaction between the *Z*-phosphine oxide (**4**) and the dialdehyde (**29**) produces the di-*Z*-nonaene (**33**) which has the same chromophore as that found in di-*Z*-ζ-carotene (**3**) from Tangerine tomato fruits.

The Wittig reaction is without doubt one of the most valuable C–C bond forming reactions available to the synthetic chemist. Examples of its use in the synthesis of all types of substituted double bonds, found in a wide range of complex natural products, are now legion.[1] Although the preparative versatility of the Wittig reaction is beyond question, its stereochemical course is often less predictable, and frequently leads to mixtures of *Z*- and *E*-geometrical isomers about the newly introduced double bond. This feature of the reaction has provoked considerable discussion regarding its general mechanism, and also much experimental work directed towards controlling the stereochemical outcome of the reaction.[1] Indeed, a range of conditions are now available for the production of largely *Z*- or *E*-*disubstituted monoenes* by the Wittig process.

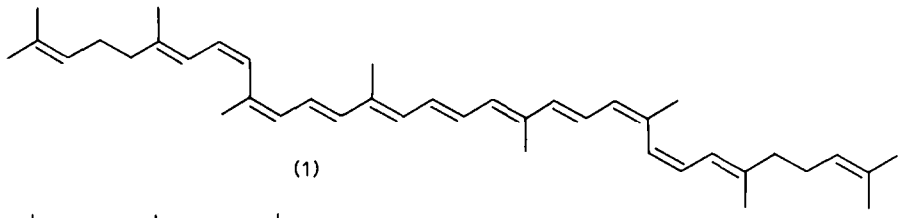
Although conditions are known for the synthesis of conjugated polyenes from α, β-unsaturated phosphoranylids and α,β-unsaturated aldehydes whereby the *Z*- or *E*-geometries in these substrates are preserved, the olefinations themselves almost invariably produce mixtures of *Z*- and *E*-isomers about the newly introduced double bond.[2] Time consuming chromatography, which is frequenntly accompanied by stereomutation and equilibration of the isomeric polyene, is then essential to separate the required geometrical isomers. The need for an alternative method to the Wittig reaction for the controlled synthesis of isomeric conjugated polyenes, which at the same time has all the desirable practical advantages of that reaction when handling polyenes (low temperature, mild base, inert atmosphere, diffuse light), is very clear.

Some four years after Wittig and Schöllkopf published their now celebrated paper describing the Wittig reaction,[3] Horner *et al.*[4] outlined the use of the corresponding diphenylphosphine oxide carbanion intermediate, as an alternative to triphenylphosphoranylide, in the synthesis of alkenes. To-day this reaction has been dubbed the Horner variant of the Wittig reaction and more generally the Horner–Wittig reaction. Although sporadic reports of the use of phosphine oxide anions in alkene synthesis appeared in the literature during the ensuing fifteen years,[5] it is not until comparatively recent that further attention has been given to the Horner–Wittig reaction as an alternative to the Wittig process in the synthesis of isomeric alkenes.

At the outset of the studies described in this paper, evidence had accrued suggesting that diphenylphosphine oxide carbanion intermediates offered convenience and many advantages over phosphoranylides for the controlled synthesis of isomeric 1,3-dienes, for example, from α,β-unsaturated phosphine oxide carbanions and aldehyde precursors.[6] Their applicability to the synthesis of higher conjugated polyenes, however, was not known. In connection with our studies on the structure and synthesis of poly-*Z*-carotenoids [e.g. prolycopene (**1**), di-*Z*-phytofluene (**2**), di-*Z*-ζ-carotene (**3**)]† found in Nature,[7] we have now explored the use of the Horner–Wittig reaction in the stereo-controlled synthesis of polyene isoprenoids of this general type. The outcome of these studies are summarised here.[9]

We began our studies with an investigation of the use of the *Z*- and *E*-phosphine oxides (**4** and **5**) in the synthesis of stereoisomers of 2, 6, 11, 15-tetramethylhexadeca-2, 6, 8, 10, 14-pentaene (**6**) by reaction with the isomeric citrals (**7** and **8**). In previous synthetic work, all six geometrical isomers of the pentaene had been prepared and fully characterised.[2] The phosphine oxides (**4** and **5**) were produced from nerol and geraniol respectively, following conversion to the corresponding allylic chlorides, reaction with diphenylphosphide, and oxidation of the resulting tertiary phosphines with hydrogen

†Throughout this paper, the *Z*- and *E*- nomenclature is used to describe the geometry of carbon-carbon double bonds.[8] Carbon–carbon double bonds of polyenes may be taken as having the *E*-geometry unless it is otherwise stated.



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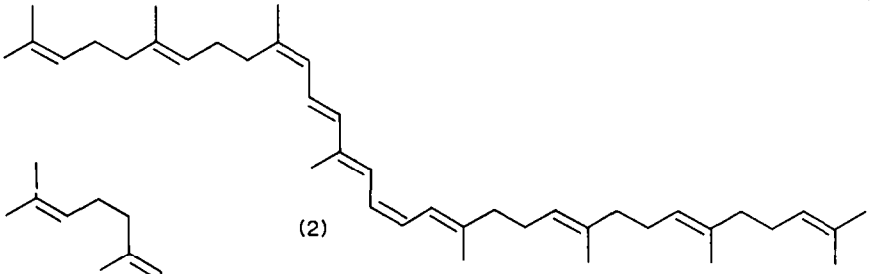

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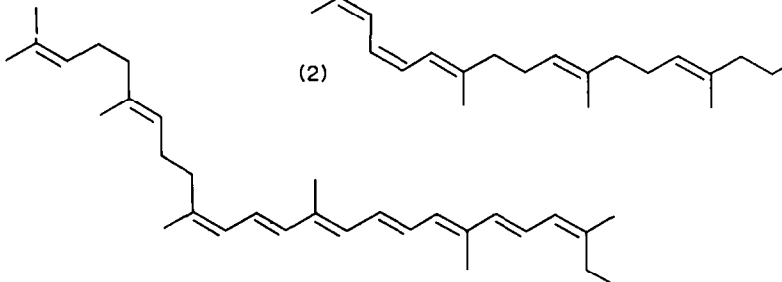


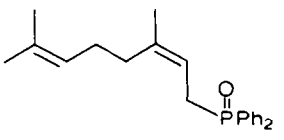
(3)

peroxide.[6a] They were clearly distinguished by mixed m.p. and NMR data.

Metallation of the individual phosphine oxides at −60° using *n*-butyl-lithium, followed by reaction with *Z*- or *E*-citral and warming to 25°, led to the corresponding isomeric pentaenes showing complete preservation of the *Z*- or *E*-geometries in the starting materials, and with >98% *E*-olefination. Thus, the phosphine oxide (**4**) and *Z*-citral led to **9**, whilst the phosphine oxide (**5**) and *Z*-citral, or the phosphine oxide (**4**) and *E*-citral both produced **10**. These results are to be contrasted with those obtained with the corresponding *Z*- and *E*-phosphonium salts (i.e **11** adnd **12**) which gave rise to the corresponding *Z*-olefination products (*Z*:*E* *ca* 1:1) concurrently.[2]

The most disappointing feature of the Horner–Wittig syntheses of the isomeric pentaenes (**6**) was the low yields recorded (10–20%) in comparison with those obtained in the corresponding Wittig reactions (*ca.* 70%). In addition, using the single-step conditions described, from each reaction we recovered up to 50% of the starting phosphine oxide, and upwards of 15% of the cyclohexadiene by-product (**13**) produced by self-condensation of citral.[10] A wide range of alternative reaction conditions (e.g . temp, 2 equivs BuLi, phase transfer methods, KOBu^t base)[6,11] were investigated in order to increase the yields in these reactions but they were singularly unsuccessful. In those instances where we were able to increase yields (≯50%), we also observed extensive stereomutation about the double bonds of the starting phosphine oxides.

Further experiments, designed to examine other fea-



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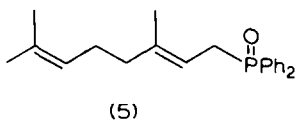

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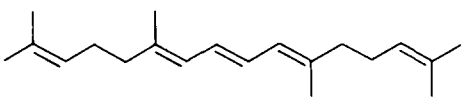

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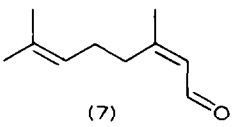

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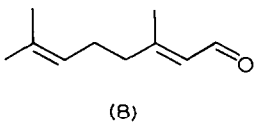

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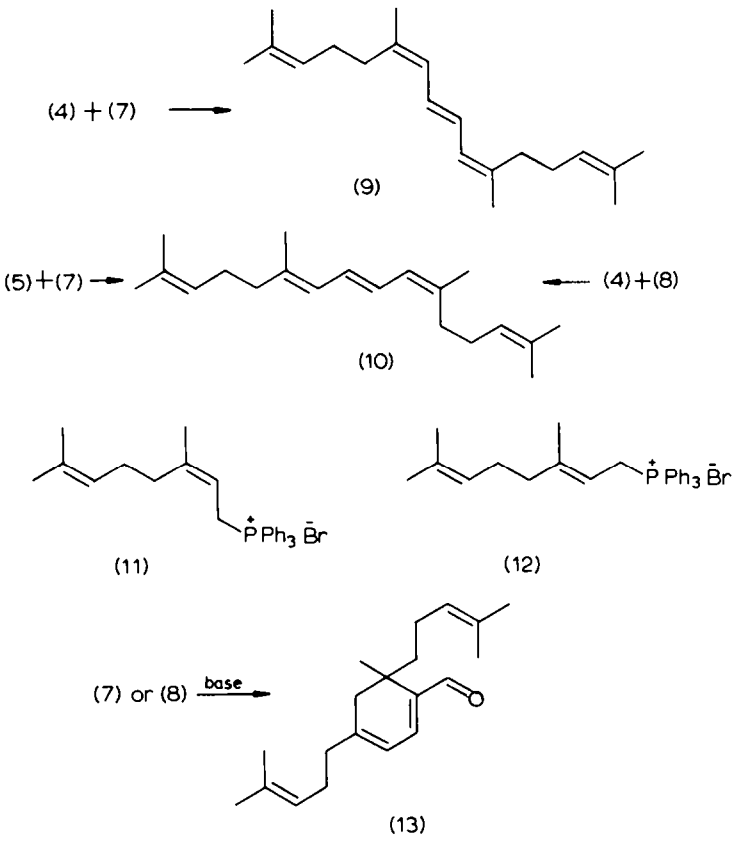
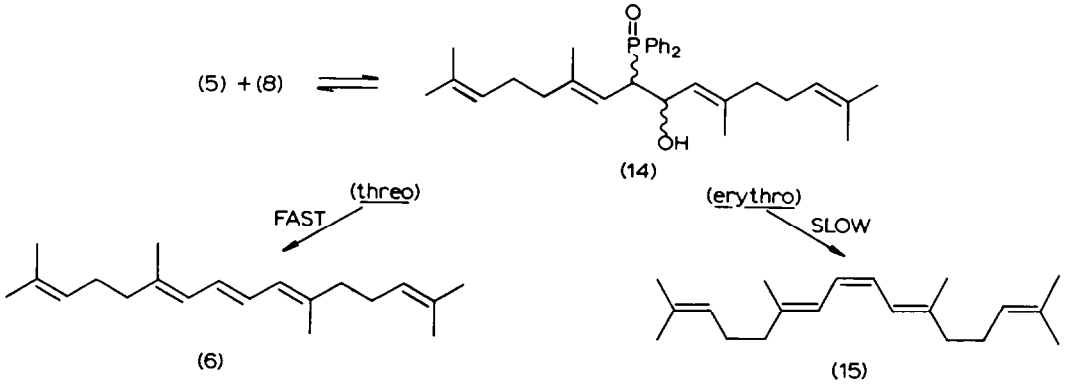


tures which might control the yield and stereochemical outcome of the olefinations, established that the isolation of only *E*-olefination products in the single-step reactions was associated entirely with the much slower rates of β-elimination from the *erythro*-β-hydroxyphosphine oxide intermediates produced in the reactions. This feature was substantiated when the *threo*- and *erythro*-intermediates (e.g. **14**) were separated from reactions quenched after short periods of time at $-60°$ and the individual intermediates treated in a separate step with sodium hydride in dimethylformamide.[12] Thus, the *E*-phosphine oxide (**5**) and *E*-citral, at $-60°$, produced a 1:1 mixture of *threo*- and *erythro*-β-hydroxyphosphine oxide intermediates (**14**) in a combined yield of 73%. Treatment of the purified *threo*-intermediate with sodium hydride in dimethylformamide then led to the all-*E*-pentaene (**6**) in 70% yield within 0.5 hr, whereas the corresponding *erythro*-β-hydroxyphosphine oxide intermediate, under the same conditions, in the same period of time, gave only a 18% yield of a mixture of the E,*Z*,*E*-triene (**15**) and the all-*E*-triene (**6**), the major product being the *E*-phosphine oxide (**5**) (Scheme 1). In a similar manner, this two-stage procedure, using the *Z*-phosphine oxide (**4**) and *E*-citral, produced (75%) a 3:2 mixture of the corresponding *threo*- and *erythro*-β-hydroxyphosphine oxide intermediates; subsequent treatment of the *threo*-intermediate then gave the *Z*-6, *E*-8, *E*-10-pentaene (**10**) in 74% yield.

The above data go some way to explaining the low yields and exclusive *E*-olefinations observed in the single-step syntheses of the isomeric pentaenes (**6**): (i) formation of the β-hydroxyphosphine oxide anion inter-



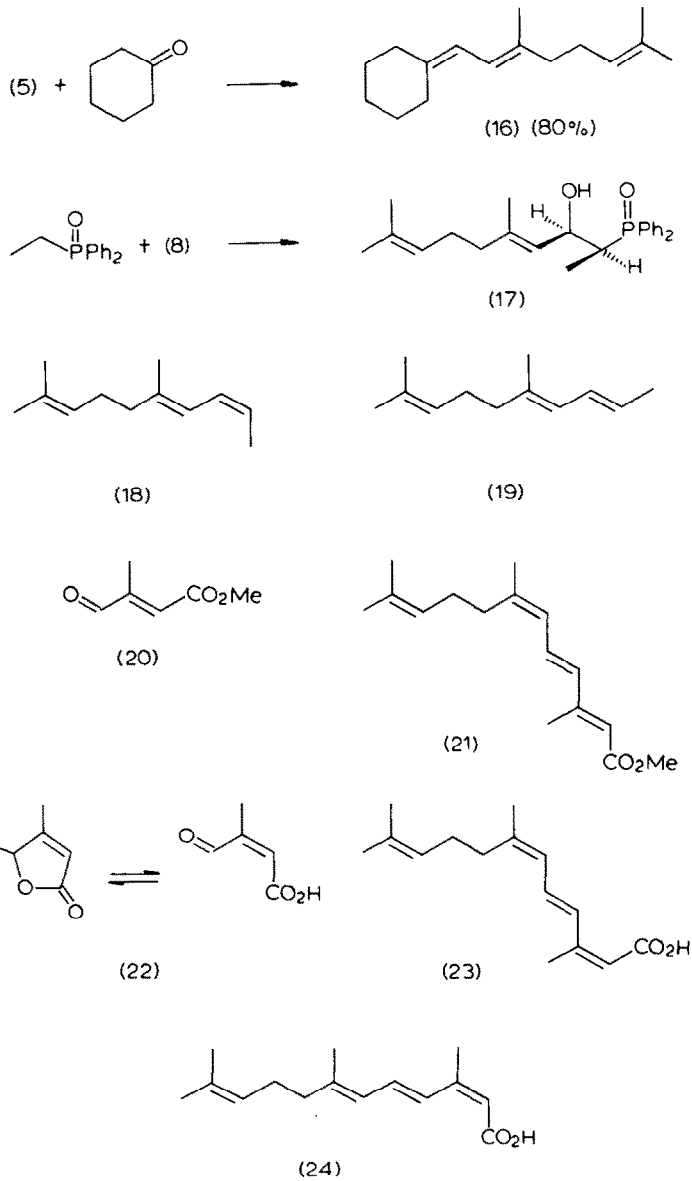
Scheme 1.

mediates is fast and reversible; this is clear from the observed accumulation of **13**, and of isomerisation of the starting phosphine oxide with time, (ii) *syn*-elimination from the *threo*-diphenylphosphine oxide anion intermediate is energetically favoured over the *erythro*-intermediate, and it is this "kinetic" effect which accounts for the observed (apparent) *E*-stereoselectivity, rather than any other effect.

The importance of the structure of the phosphine oxide and the carbonyl compound in determining the yield and stereochemical outcome of the Horner-Wittig reaction was further illustrated in two other instances.

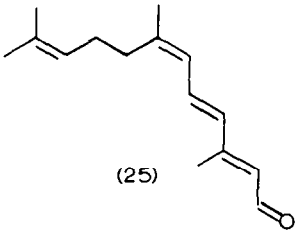
Thus, a Horner-Wittig reaction between the *E*-phosphine oxide (**5**) and cyclohexanone led, in a single-step, to the triene (**16**), isolated in 79% yield.[13] Here the elimination from the intermediate β-hydroxyphosphine oxide anion is clearly very fast, even at 0°. By contrast, reaction between ethyldiphenylphosphine oxide and *E*-citral at 25° led to almost entirely the *erythro*-β-hydroxyphosphine oxide intermediate (**17**) accompanied by a small amount of the corresponding *threo*-intermediate.[14] None of the isomeric trienes (**18** and **19**) were detected in the crude mixture, although these could be produced in separate steps upon treatment of the *erythro*- and *threo* intermediates with NaH in DMF. The stereochemical outcome of this particular reaction is not dissimilar to the corresponding Wittig reaction using 'non-stabilised' primary phosphoranylids and aldehydes which lead to predominantly *Z*-olefination products *via* irreversible betaine formation.[1,15] The total absence of elimination from the intermediate β-hydroxyphosphine oxide anions at 25° in this reaction is most interesting and quite surprising.

Having established the use of the single-step Horner-Wittig reaction in the synthesis of *E*-disubstituted double bonds set within a conjugated polyene isoprenoid system, we turned our attention to longer functionalised polyenes (e.g. **21**, **31**) required for elaboration to the di-*Z* pentaene and heptaene chromophores (**28** and **33**) present in phytofluene (**2**) and ζ-carotene (**3**) respectively found



in fruit of the Tangerine tomato *Lycopersicon esculentum* var.

Thus, metallation of the *Z*-phosphine oxide (**4**) followed by reaction with methyl 3-formylbut-*E*-2-enoate (**20**)[16] led, in a single step, to the *E*-2, *E*-4, *Z*-6-tetraenoate (**21**) in 34% yield. In a similar manner, Horner-Wittig reactions between **4** and the *Z*-aldehyde (**22**),[17] and between **22** and the *E*-phosphine oxide (**5**) produced the corresponding *Z*-2, *E*-4, *Z*-6-(**23**) and *Z*-2, *E*-4, *E*-6 (**24**) tetraenoic acids respectively. The exclusive *E*-olefinations observed in these single-step reactions were obtained at the expense of low overall yields



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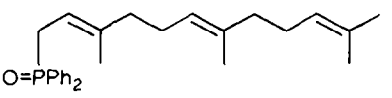

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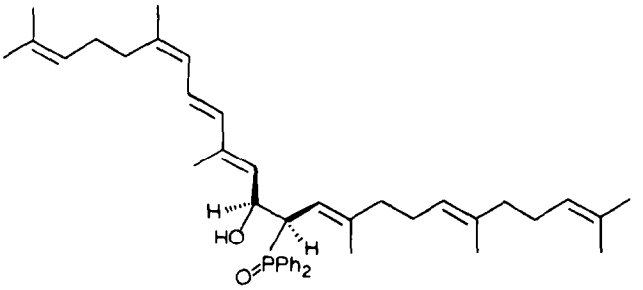

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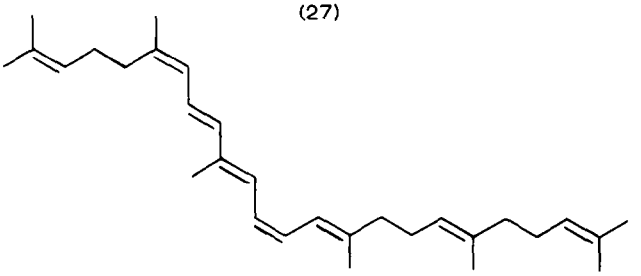

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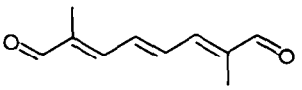

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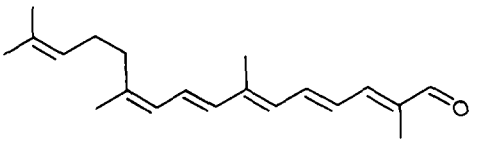

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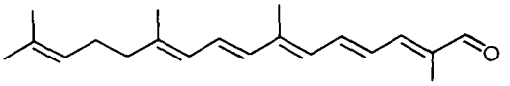

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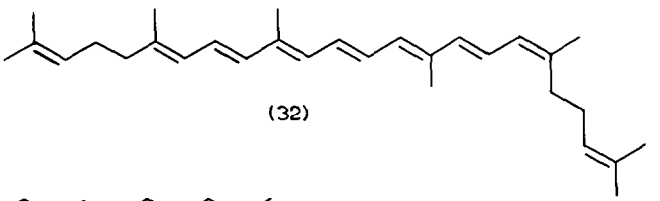

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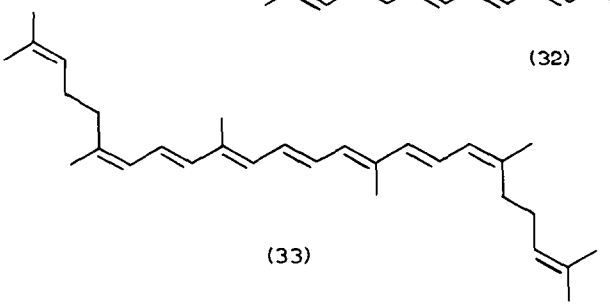

(33)

(>34%). The corresponding Wittig reactions, using both **11** and **12**, produced the acids **23** and **24** and the ester **21** in higher overall yields (*ca.* 75%), but upwards of 40% *Z*-olefinations were observed concurrently.

In separate studies, the *E*-2, *E*-4, *Z*-6-ester (**21**) was converted into the di-*Z*-octaene (**28**) following conversion to the tetraenal (**25**), Horner–Wittig reaction with farnesyl phosphine oxide (**26**), and treatment of the purified *erythro*-β-hydroxyphosphine oxide (**27**) with sodium hydride in dimethylformamide. The di-*Z*-octaene (**28**) showed closely similar spectral data to those found in natural di-*Z*-phytofluene (**2**) from Tangerine tomato fruits.[7]

Although the Horner–Wittig syntheses of the hexaenal (**30**) and the nonaene (**33**), from **4** and the dialdehyde (**29**), proceeded in reasonable yield and with almost complete *E*-olefination, they were accompanied by isomers resulting from stereomutation (20–30%) about the double bond in the starting phosphine oxide (**4**). Thus, condensation between two mole equivalents of the *Z*-phosphine oxide (**4**) and the dialdehyde (**29**), led (33%) to the *Z*-10-hexaenal (**30**) accompanied by *ca.* 30% of the all-*E*-isomer (**31**). Similarly, reaction between the all-*E*-hexaenal (**31**) and **4** produced (70%) the *Z*-6-nonaene (**32**) contaminated with *ca.* 25% of the all-*E*-nonaene. Interestingly, the Horner-Wittig reaction between **29** and **4** mole equivalents of the *Z*-phosphine oxide (**4**) led, in one step, to the di-*Z*-nonaene (**33**) in 86% yield; once again however, the condensation was accompanied by stereomutation about the double bond in **4**. The C_{40}-prenylogue of **33** (i.e. di-*Z*-ζ-carotene **3**) has been found, along with **1** (and **2**) in Tangerine tomato fruits.[7]

The present results, and the synthesis of the di-*Z*-polyene (**28**) in particular, fully demonstrate the scope of the Horner–Wittig reaction in the controlled synthesis of *E*- and *Z*-disubstituted double bonds set within a conjugated polyene isoprenoid framework. Although overall yields in the *single-step* Horner–Wittig reactions are not always high, this feature has to be offset against the almost exclusive *E*-olefinations observed in all the cases studied; concurrent stereomutation about the double bonds of α,β-unsaturated phosphine oxides can present problems. An added bonus associated with the Horner–Wittig reaction over the Wittig reaction is the possibility of isolation of the intermediate β-hydroxyphosphine oxides (≡ "betaines"). Subsequent elimination from the separated *erythro*-intermediates then permits the synthesis of *Z*-disubstituted double bonds (see synthesis of **28**), thus avoiding the tedious chromatography often necessary in the purification of *Z*- and *E*-isomers resulting from the corresponding Wittig reactions.

EXPERIMENTAL

Solvents were redistilled before use. Solns were dried over $MgSO_4$ and concentrated under reduced pressure. Unless otherwise stated, preparative chromatography was carried out on columns of silica gel (Silica Woelm TSC) and preparative thin-layer chromatography (plc) was performed on 40 × 40 cm silica gel plates (Fluka Kieselgel HF_{254}).

Wittig and Horner-Wittig olefinations were carried out in dry solvents in the dark and under an atmosphere of dry N_2, and the reactions were worked-up in subdued light. Polyenes were never allowed to remain in contact with the air, and were only left in soln or in contact with active chromatographic surfaces for the minimum length of time before spectral data were recorded. In addition, polyenes were never heated above room temp and, when necessary, were stored under vacuum, at 0°, and in the dark.

Polyenes have been numbered according to the I.U.P.A.C. recommendations, and C–C double bonds may be taken as having the *E*-configuration unless otherwise stated.

Z-(3,7-dimethylocta-2,6-dienyl)diphenylphosphine oxide (**4**)

Methanesulphonyl chloride (22.4g) was added during 15 min to a stirred soln of nerol (15 g) in dry pentane (280 ml) at −5°. The stirred soln was treated with a soln of pyridine (15.4 g) in pentane (70 ml) during 15 min, and the mixture was then allowed to warm to room temp. The mixture was stirred at 25° for 5 hr. and then the pentane was decanted from the viscous pink residue, washed successively with 5% HCl, $NaHCO_3$ aq and water, then dried. Evaporation of the pentane left *Z*-1-chloro-3,7-dimethylocta-2,6-diene (12.90 g, 77%) as an almost colourless oil, ν_{max} 1660, 845, 680 cm^{-1}, τ 4.57 (t, *J* 8, :C*H*.CH_2Cl), 4.89 (br, Me_2C:C*H*), 5.94 (d, *J* 8, CH_2Cl), 7.86–7.89 (m, 4H), 8.23 (:C*Me*), 8.3 (:C*Me*), 8.38 (:C*Me*); *m/e* 174 (0.2%, *M* for ^{37}Cl), 172 (0.4%; M for ^{35}Cl), 136 (97%, M-HCl), 121 (100%). (Found: M^+ 172.1017. Calc. for $C_{10}H_{17}Cl$: 172.1019).

A soln of the chloride (12.8 g) in dry THF (35 ml) was added to a stirred red-coloured soln of lithium diphenylphosphide [from n-BuLi (47 ml of 1.58 M in n-hexane) and diphenylphoshine (13.8 g)] in THF (200 ml) at 0°. The red-colour of the anion was discharged almost immediately, and after 15 min the mixture was diluted with water (2 ml). Evaporation of the THF left a residue which was dissolved in $CHCl_3$ and washed successively with 15 volume H_2O_2, Na_2SO_3aq, 5% HCl, $NaHCO_3$aq and water. Evaporation of the dried $CHCl_3$ solution left a crystalline residue which recrystallised from benzene-n-hexane to give the *phosphine oxide* (15.2 g, 60%) as colourless needles, m.p. 93.5–94°, ν_{max} (KBr) 1180, 1120, 735, 715, 690 cm^{-1}, τ 2.2–2.65 (m, PPh_2), 4.82 (apparent q, *J* 8, :C*H*.CH_2P), 5.02 (br, Me_2 C:C*H*), 6.94 (dd, *J* 14 and 8, CH_2-P), 8.08–8.11 (m, CH_2CH_2), 8.34 (2 × :C*Me*), 8.44 (:C*Me*), δ 17.66 (C-7-Me-*Z*), 23.45 (C-3-Me), 25.61 (C-7-Me-*E*), 26.08 (C-5), 30.55 (d, J_{CP} 72, C-1), 31.99 (C-4), 112.63, 112.92, 123.91, 128.18, 128.59, 130.76, 131.05, 131.52, 134, 91, 140.64, 141.11 p.p.m.; *m/e* 338 (100%, M), 269 (99%, M-C_5H_9), (Found: C, 78.1; H, 8.1. M^+, 338.1821. $C_{22}H_{27}OP$ requires: C, 78.1; H, 8.0%. M^+, 338.1799).

E-(3,7-Dimethylocta-2,6-dienyl)diphenylphosphine oxide (**5**)

The phosphine oxide was prepared from geraniol, in an identical manner to that described for the preparation of the corresponding *Z*-phosphine oxide from nerol.

Chlorination of geraniol led to *E*-1-chloro-3,7-dimethylocta-2,6-diene (74%), ν_{max} (film) 1660, 845, 675 cm^{-1}, τ 4.57 (t, *J* 8, :C*H*.CH_2Cl), 4.92 (br, Me_2C:C*H*), 5.92 (d, *J* 8, CH_2Cl), 7.93 (m, 4H), 8.27 (:C*Me*), 8.31 (:C*Me*), 8.39 (:C*Me*); *m/e* 174 (0.2%, M for ^{37}Cl), 172 (0.5%, M for ^{35}Cl), 136 (82%, M-HCl), 121 (100%), (Found: M^+, 172.1013. Calc. for $C_{10}H_{17}Cl$: 172.1019). Reaction with lithium diphenylphosphide, followed by oxidation then gave the phosphine oxide (85%) which crystallised from benzene-n-hexane as colourless needles, m.p. 112.5–114° (lit.[20] m.p. 113–114°), ν_{max} (KBr) 1180, 1120, 740, 715, 695 cm^{-1}, τ 2.20–2.68 (m, PPh_2), 4.77 (apparent q, *J* 8, :C*H*CH_2P), 5.02 (br, Me_2C:C*H*), 6.93 (dd, *J* 15 and 8, CH_2P), 8.02–8.04 (m, CH_2CH_2), 8.36 (:C*Me*), 8.45 (:C*Me*), 8.55 (d, *J* 4, *Me*C:CHCH_2P, δ 16.37 (C-3-Me), 17.60 (C-7-Me-*Z*), 25.61 (C-7-Me-*E*), 26.43 (C-5), 30.82 (d, J_{CP} 71, C-1), 39.71 (C-4), 112.16, 112.51, 123.86, 128.12, 128.59, 130,81, 131, 17, 131.34, 131.57, 134.85, 140.64, 141.11 p.p.m.; *m/e* 338 (100%, M), 269 (99%, M-C_5H_9), (Found: C, 78.0; H, 8.1. M^+, 338.1828. Calc. for $C_{22}H_{27}OP$: C, 78.1; H, 8.0%; *M*, 338.1799).

Synthesis of polyene isoprenoids by the Horner-Wittig reaction

(a) *Single-stage reactions—General procedure.* A soln of n-BuLi (q equiv) in hexane was added dropwise over 5 min to a stirred soln of *Z*- or *E*- (3,7-dimethylocta-2,6-dienyl)diphenylphosphine oxide (6-8 m mole) in dry THF (100 ml) at −60° under N_2. The resulting red-coloured soln was stirred at −60° for 0.5 hr, and then the aldehyde (1 equiv) in THF (10 ml) was introduced over 5 min. The mixture was allowed to warm to room temp, then stirred at room temp for 3 hr, diluted with water and extracted with n-hexane. The combined hexane extracts were dried and evaporated. Chromatography of the residue on silica gel gave the

isomerically pure polyenes. The stereochemistry of some of the polyenes was established by comparison of spectral data with those of authentic isomers prepared previously.[2]

Two-stage reactions—General procedure. A soln of n-BuLi (1 equiv) in hexane was added dropwise over 5 min to a stirred soln of *Z*- or *E*- (3,7-dimethylocta-2,6-dienyl)diphenyl phosphine oxide (6-8 m mole) in dry THF (100 ml) at −60° under N_2. The resulting red-coloured soln was stirred at −60° for 0.5 hr, and then the aldehyde (1 equiv) in THF (10 ml) was introduced over 5 min. The mixture was immediately diluted with water (at −60°) and then extracted with $CHCl_3$. The combined extracts were washed with water, then dried and evaporated. Chromatography of the residue in 1:1 n-hexane-EtOAc on silica gel then gave the pure *erythro*- and *threo*-β-hydroxyphosphine oxide intermediates. A solution of the *erythro*- or *threo*-β-hydroxyphosphine oxide (0.4 m mole) in dry DMF (10 ml) was added to a stirred suspension of NaH (1.5 m mole) in dry DMF (10 ml) at 0°, and the mixture was allowed to warm to room temp. Water was added, and the mixture was extracted with hexane. Evaporation of the combined hexane extracts and chromatography of the residue in $CHCl_3$ on silica gel gave the isomerically pure polyenes whose stereochemistries were established from their spectral data.

Geometrical isomers of 2,6,11,15-tetramethylhexadeca-2,6,8,10,14-pentaene (**6**)

The individual isomers were purified by chromatography in chloroform.

(a) By the general single-stage procedure, reaction between the *E*-phosphine oxide (**5**) and the *E*-aldehyde (**8**) led to the all-*E*-pentaene (**6**) (10%) contaminated with small amounts of th *E*-**6**, *Z*-**8**, *E*-**10**-(**15**) and *Z*-**6**, *E*-**8**, *E*-**10**-(**0**) isomers.

(b) By the general single-stage procedure, reaction between the *E*-phosphine oxide (**5**) and the *Z*-aldehyde (**7**) gave the *Z*-**6**, *E*-**8**, *E*-**10**-pentaene (17%) containing small amounts (<4%) of the *Z*-**6**, *Z*-**8**, *E*-**10**-isomer. Chromatography also separated 4,6-*bis*-(4-methylpent-3-en-1-yl)-6-methylcyclohexa-1,3-diene-carbaldehyde (**13**) (8%) which showed spectral data identical to those reported previously.[10]

(c) By the general single-stage procedure but using 2 equivs *n* BuLi reaction between the *Z*-phosphine oxide (**4**) and the *E*-aldehyde (**8**) gave the *Z*-**6**, *E*-**8**, *E*-**10**-pentane (46%), contaminated with the all-*E*-pentaene (*ca.* 30%) and the *Z*-**6**, *Z*-**8**, *E*-**10**-pentaene (*ca.* 6%). A similar ratio of isomers was obtained when the *E*-aldehyde was added at 0° instead of at −60°.

When an equivalent of n-BuLi was added to a *mixture* of the *Z*-phosphine oxide and the *E*-aldehyde at −60°, the usual work-up procedure gave the *Z*-**6**, *E*-**8**, *E*-**10**-pentaene (22%) uncontaminated with geometrical isomers.

(d) By the general single-stage procedure, reaction between the *Z*-phosphine oxide (**4**) and the *Z*-aldehyde (**7**) gave *Z*-**6**, *E*-**8**, *Z*-**10**-pentaene (12%) contaminated with the *Z*-**6**, *E*-**8**, *E*-**10**-pentaene (*ca.* 14%).

(e) By the general two-stage procedure, reaction between the *E*-phosphine oxide (**5**) and the *E*-aldehyde (**8**) led to the *erythro*-β-hydroxyphosphine oxide (35%), a white solid, ν_{max} 3400, 1665, 895, 825 cm^{-1}, τ 1.87–2.63 (m, 10H), 4.31 (dd, *J* 12 and 7, :C*H*OH), (4.65 (d, *J*9, :C*H*COH), 4.80–5.2 (m, 3H), 5.41 (O*H*), 6.68 (apparent dd, J 12 and 8, –C*H*P), 8.01 (br, CH_2CH_2), 8.33 (2×C*Me*), 8.4 (2×C*Me*), 8.5 (*C*-11-CH_3), 8.56 (d, *J* 3, C-6-CH_3), and the *threo*-β-hydroxyphosphine oxide (38%) a white solid, ν_{max} (KBr) 3380, 1650, 885, 825 cm^{-1}, τ 1.91–2.57 (m, 10H), 4.96 (br, Me_2C:C*H*), 4.72, 4.81, 4.87, 5.04, 5.21, 5.29 (m, 4H, :C*H*.C*H*O*H* and C*H*CP), 6.47 (apparented *J* 12 and 9, –C*H*P), 8.02–8.05 (m, 4H), 8.33 (2×:C*Me*), 8.4 (2×;C*Me*), 8.47 (C-11-CH_3), 8.51 (d, *J* 3, C-6-CH_3).

Treatment of the *erythro*-β-hydroxyphosphine oxide (0.26 g) with NaH in DMF, according to the general procedure, gave: (i) the *E*-**6**, *Z*-**8**, *E*-**10** pentaene (18%) contaminated with the all-*E*-pentaene (*ca.* 10%), and (ii) the *E*-phosphine oxide (**5**; 0.05 g),

Treatment of the *threo*-β-hydroxyphosphine oxide (0.2 g) with NaH in DMF, according to the general procedure gave the all-*E*-pentaene **6** (70%) uncontaminated with geometrical isomers.

(f) By the general two-stage procedure, reaction between the *Z*-phosphine oxide (**4**) and the *E*-aldehyde (**8**) led to a 2:3 mixture of *erythro*- and *threo*-β-hydroxyphosphine oxides (74%) from which the *threo*-diastereomer was purified by crystallisation, m.p. 90–92°, ν_{max} (KBr) 3380, 885, 815 cm^{-1}, τ 2.03–2.58 (m, 1OH), 4.82–5.39 (m, :C*H* and *HCOH*), 6.52 (td, *J* 11 and 8, CHP), 8.09–8.16 (m; 8H), 8.35, 8.40, 8.45, 8.51 (6×:C*Me*).

Treatment of the *threo*-β-hydroxyphosphine oxide (0.056 g) with NaH in DMF, according to the general procedure gave: (i) the *Z*-**6**, *E*-**8**, *E*-**10**-pentaene (23 mg, 74%), and (ii) the *Z*-phosphine oxide. (5 mg).

E-3,7-Dimethylocta-2,6-dienylidenecyclohexane (**16**)

By the general single-stage procedure, reaction between the *E*-phosphine oxide (**5**) and cyclohexanone led to the *E-triene* (79%) as a colourless oil, λ_{max} (EtOH) 234 inf., 242, 249, 257 inf., nm (ε 22,500, 29,700, 33,000, 24,400), ν_{max} (film) 1620, 985, 865, 855 cm^{-1}, τ 3.93 (d, *J* 12, :C*H*.CH:), 4.09 (d, *J* 12, :CH.C*H*), 4.87 (br, Me_2C:C*H*), 7.72–7.9 (m, 8H), 8.23 (:C*Me*), 8.3 (:C*Me*), 8.37 (:C*Me*), 8.37–8.44 (m, 6H). δ 16.37 (C-3-Me), 17.72 (C-7-Me-*Z*), 25.67 (C-7-Me-*E*), 27.02, 27.02, 28.77, 29.06, and 37.72 (ring methylenic carbon nuclei), 27.84 (C-5), 40.47 (C-4), 118.24 (C-1 or C-2), 120.17 (C-2 or C-1), 124.32 (C-6), 131.28 (C-7), 135.96 (ring olefinic carbon nucleus), 140.70 (C-3) p.p.m., *m/e* 218 (22%, M), 149 (100%, M-C_5H_9), (Found: M^+ 218.2041. $C_{16}H_{26}$ requires *M*, 218.2034).

E-**6**, *Z*-**8** and E-**6**, *E*-**8**-*Isomers* of *2,6-dimethyldeca-2,6,8-triene* (**18** *and* **19**)

By the general two stage procedure, reaction between ethyldiphenylphosphine oxide[21] and *E*-citral (**8**) led to the *erythro* β-hydroxyphosphine oxide (**17**; 55%), a white solid, ν_{max} (KBr) 3390, 1180, 1115, 1075, 1010, 900, 740, 720, 695 cm^{-1}, τ 2.05–2.6 (m, PPh_2), 4.66 (d, *J* 8, C-4-H), 4.96 (br, C-8-H), 4.96 (br, C-8-H), 5.22 (apparent q, *J* 9, C*H*OH), 5.88 (OH), 7.67 (m, *J* 7, CHP), 8.01 (br, CH_2CH_2), 8.33 (C-9-Me-*E*), 8.41 (C-9-Me-*Z*), 8.61 (C-5-Me), 8.77 (dd, *J* 16 and 7, C-2-Me), *m/e* 364 (2%, M), 313 (4% M-C_5H_9), 230 (100%, M-citral), (Found: M^+, 382.2056. $C_{24}H_{31}O_2P$ requires: *M*, 382.2062), and the *threo*-β-hydroxyphosphine oxide (16%), a white solid, ν_{max} (film) 3350, 1670, 1175, 1070, 1010, 890, 755, 720, 695 cm^{-1}, τ 2.2–2.7 (m, PPh_2), 4.85 (d, *J* 9, C-4-H), 5.02 (br, C-8-H), 5.36 (br, OH), 5.40 (apparent q, *J* 9, C*H*OH), 7.33 (apparent sextet, *J* 7, CHP), 8.06 (br, CH_2CH_2), 8.38 (C-9-Me-*E*), 8.46 (C-9-Me-Z), 8.50 (C-5-Me), 9.05 (dd, *J* 17 and 7, C-2-Me).

Treatment of the *threo*-β-hydroxyphosphine oxide (87 mg) with with NaH in DMF, according to the general procedure gave th *E*-**6**, *Z*-**8**-triene (28 mg, 36%) as a colourless liquid, ν_{max} (film) 825, 720 cm^{-1}, τ 3.66–4.04 (2H, m) and 4.44–4.74 (1H, m) (C-7-H, C-8-H, C-9-H), 4.89 (C-3-H), 7.88–7.90 (m, CH_2CH_2), 8.25 (C-6-Me), 8.28 (d, *J* 6, C-10-H), 8.31 (C-2-Me-*E*), 8.39 (C-2-Me-*Z*), δ 13.16 (C-10), 16.43 (C-6-Me), 17.66 (C-2-Me-Z), 25.67 (C-2-Me-*E*), 26.78 (C-4), 40.29 (C-5), 119.70 (C-7), 123.74, 125.67 (C-8, C-9), 124.15 (C-3), 131.52 (C-2), 138.24 (C-6) ppm.

Treatment of the *threo*-β-hydroxyphosphine oxide (87 mg) with NaH in DMF, according to the general procedure gave the *E*-**6**, *E*-**8**-triene (25 mg, 67%) as a colourless liquid. ν_{max} (film) 965, 825 cm^{-1}, τ 3.73 (dd, *J* 15 and 11, C-8-H), 4.20 (d, *J* 11, C-7-H), 4.38 (dq, *J* 15 and 6, C-9-H), 4.89 (br, C-3-H), 7.91–7.93 (m, CH_2CH_2), 8.23 (d, *JJ* 6, *C*-10-H), 8.26 (C-6-Me), 8.31 (C-2-Me-*E*), 8.39 (C-2-Me-*Z*). δ 16.49 (C-6-Me), 17.66 (C-2-Me-*Z*), 18.30 (C-10), 25.67 (C-2-Me-*E*), 26.72 (C-4), 39.94 (C-5), 124.21 (C-3), 124.73, 126.60, 128.12 (C-7, C-8, C-9), 131.40 (C-2), 135.79 (C-6) ppm.

Isomers of 3, 7, 11-*trimethyldodeca-2,4,6,10-tetraenoic acid* (**24**) *and its methyl ester*

(a) By the general single-stage procedure the *Z*-phosphine oxide **4** (2.23 g) and 4-hydroxy-3-methylbut-2-enolide (0.68 g)[17] gave the *Z*-2, *Z*-6 tetraenoic acid (**23**) (0.14 g, 10%) which was purified by chromatography in 1:1 EtOAc-n-hexane and showed λ_{max} ($CHCl_3$) 325 nm, ν_{max} (KBr) 3500–2400 (O–H), 1675, 1640, 1605, 1580, 975, 950, 880, 725 cm^{-1}, τ-0.22, (br, CO_2H), 2.37 (d, *J* 16, C-4-H), 3.15 (dd, *J* 16 and 11, C-5-H), 3.94 (d, *J* 11, C-6-H),

4.36 (C-2-H), 4.87 (br, C-10-H), 7.79–7.85 (m, CH_2CH_2), 7.94 (C-3-Me), 8.14 (C-7-Me), 8.32 (C-11-Me-*E*), 8.38 (C-11-Me-*Z*). δ 17.66 (C-11-Me-*Z*), 21.17 (C-3-Me), 24.33 (C-7-Me), 25.67 (C-11-Me-*E*), 26.90 (C-9), 32.92 (C-8), 115.49 (C-2), 123.62 (C-10), 126.55, 127.25, 132.22, 132,92, 144.91, 153.80 (C-3), 171.87 (C-1) ppm, *m/e* 234 (18%, M), 165 (27%, M-C_5H_9), 147 (100%), (Found: M^+, 234.1638. $C_{15}H_{22}O_2$ requires: *M*, 234.1620).

A corresponding reaction between neryltriphenylphosphonium bromide (**11**)[2] and 4-hydroxy-3-methylbut-2-enolide in THF at 25° produced the *Z*-**2**, *Z*-**6**-tetraenoic acid (70%) contaminated by the all-*Z*-isomer (~40%) characterised as its Me-ester, τ 3.17 (d, *J* 11, C-4-H), 3.57 (apparent t, *J* 11, C-5-H), 3.85 (d, *J* 11, C-6-H), 4.34 (C-2-H), 4.90 (br, C-10-H), 6.33 (CO_2Me), 7.82–7.86 (m, CH_2CH_2), 7.86 (C-3-Me), 8.17 (C-7-Me), 8.33 (C-11-Me-*E*), 8.40 (C-11-Me-*Z*).

(b) By the general two stage procedure, the *E*-phosphine oxide **5** (2.03 g) and 4-hydroxy-3-methylbut-2-enolide (0.76 g) gave the *Z*-2-tetraenoic acid **24** (7%) which was purified by chromatography in 1:1 EtOAc-n-hexane and showed λ_{max} ($CHCl_3$) 322 nm., ν_{max} (KBr) 3600–2400 (O–H), 1670, 1630, 1605, 1575, 975, 940, 870, 715 cm^{-1}, τ ~ 1.25 (br, CO_2H), 2.34 (d, *J* 15, C-4-H), 3.11 (dd, *J* 15 and 11, C-5-H), 3.90 (d, *J* 11, C-6-H), 4.35 (C-2-H), 4.89 (br, C-10-H), 7.84–7.87 (m, CH_2CH_2), 7.93 (C-3-Me), 8.16 (C-7-Me), 8.32 (C-11-Me-*E*), 8.39 (C-11-Me-*Z*), δ 17.25 (C-7-Me), 17.72 (C-11-Me-*Z*), 21.23 (C-3-Me), 25.73 (C-11-Me-*E*), 26.55 (C-9), 40.35 (C-8), 115.38 (C-2), 123.62 (C-10), 125.67, 127.42, 131.98, 133.21, 144.97, 154.03 (C-3), 171.98 (C-1), ppm; *m/e* 234 (51%, M), 166 (49%), 165 (49%, M–C_5H_9), 147 (100%), (Found: M^+ 234.1620. Calc. for $C_{15}H_{22}O_2$, *M* 234.1620).

A corresponding reaction between geranyltriphenylphosphonium bromide (**12**)[2] and 4-hydroxy-3-methylbut-2-enolide in THF at 25° produced the *Z*-2-tetraenoic acid (60%) contaminated by the *Z*-**2**, *Z*-**4**-isomer (~40%) characterised as its Me-ester.[2]

(c) By the general single-stage procedure, the *Z*-phosphine oxide **4** (3.4 g) and methyl 3-formylbut-*E*-2-enoate (1.4 g)[16] gave the *Z*-6 tetraenoete **21** (0.85 g, 34%) which was purified by chromatography in 1:4 EtOAc-n-hexane and showed λ_{max} (n-hexane) 297 inf., 308, 318 (inf.) nm (ε 28600, 36500, 30,900), ν_{max} (film) 1705, 1605, 960, 925, 880, 830, 735 cm^{-1}, τ 3.22 (dd, *J* 15 and 11, C-5-H), 3.93 (d, *J* 15, C-4-H), 4.11 (d, *J* 11, C-6-H), 4.31 (C-2-H), 4.94 (br, C-10-H), 6.35, (CO_2Me), 7.69 (d, *J* 1, C-3-Me), 7.81–7.89 (m, CH_2CH_2), 8.16 (C-7-Me), 8.33 (C-11-Me-*E*), 8.40 (C-11-Me-*Z*), δ 13.86 (C-3-Me), 17.66 (C-11-Me-*Z*), 24.27 (C-7-Me), 25.73 (C-11-Me-*E*), 26.96 (C-9), 32.98 (C-8), 50.82 (CO_2CH_3), 117.54, 123.68, 125.84, 130.99, 132, 28, 133.15, 144.03, 153.21 (C-3), 167.54 (C-1) ppm, *m/e* 248 (16%, M), 182 (73%), 151 (93%), 150 (84%), 119 (100%), (Found: M^+, 248.1790. $C_{16}H_{24}O_2$ requires: *M*, 248.1776).

A corresponding reaction between neryltriphenylposphonium bromide and methyl 3-formylbut-*E*-2-enoate in THF at 25° produced the *Z*-6-tetraenoate (74%) contaminated by the *Z*-4, *Z*-6-tetraenoate (~40%), δ 19.18 (C-3-Me), 24.44 (C-7-Me), 32.34 (C-8), ppm. Attempts to separate the isomers on $AgNO_3$-impregnated columns and by hplc were unsuccessful.

Isomers of 2,6,10,15,19,23-*Hexamethyltetracosa*-2,6,8,10,12,14,-16,18,22-*nonaene* (**32**) *and* 2,7,11,15-*Tetramethylhexadeca*-2,4,6,8,10,14-*hexaene*-1-*al* (**31**)

The isomers of the polyenes were prepared by both the single-stage and two-stage reactions. Solns of the polyenes were extracted into ether, and the isomers were purified by chromatography in chloroform.

(a) By the general two-stage procedure, the *E*-phosphine oxide **5** (4 m mole) and all-*E*-2,7-dimethylocta-2,4,6-trien-1,8-dial (2 m mole)[19] gave the all-*E*-nonaene (22%) as a red-orange waxy solid, τ 8.06 (C-10-Me and C-15-Me), 8.18 (C-6-Me and C-19-Me), 8.30 (C-2-Me and C-23-Me), 8.37 (C-2'-Me and C-23'-Me). δ 12.75 (C-10-Me and C-15-Me), 16.9 (C-6-Me and C-19-Me), 17.66 (C-2'-Me and C-23'-Me), 25.67 (C-2-Me and C-23-Me), 26.72 (C-4 and C-21), 40.29 (C-5 and C-20) ppm [contaminated with the corresponding *Z*-6 and *Z*-6, *Z*-18-isomer (*ca.* 20%).], M^+ 404.3459 Calc. for $C_{30}H_{44}$, *M* 404.3443.

A corresponding reaction between geranyltriphenylphosphonium bromide (2.7 m mole) and the all-*E*-dial **29** (1.2 m mole), in THF at 0°, produced the all-*E*-nonaene (79%) contaminated by the *Z*-**8** and *Z*-**8**, *Z*-**16**-isomer (*ca.* 40%), τ 7.96 (C-10-Me and C-15-Me), 8.21 (C-6-Me and C-19-Me), 8.3 (C-2-Me and C-23-Me), 8.37 (C-2-Me and C-23-Me) ppm.

(b) By the general, one-stage procedure, the *Z*-phosphine oxide **4** (8.0 m mole) and the all-*E*-aldehyde **29** (2 m mole) gave the *Z*-**6**, *Z*-**18**-nonaene (87%) as an orange-red waxy solid, τ 8.06 (C-10-Me and C-15-Me), 8.17 (C-6-Me and C-19-Me), 8.30 (C-2-Me and C-23-Me), 8.37 (C-2-Me and C-23-Me), δ 12.75 (C-10-Me and C-15-Me), 17.66 (C-2-Me and C-23-Me), 24.15 (C-6-Me and C-19-Me), 25.73 (C-2-Me and C-23--Me), 26.90 (C-4, C-21), 32.81 (C-5 and C-20) ppm contaminated with the corresponding *Z*-6 and all-*E*-nonaene (*ca.* 40%). A similar proportion of isomers was obtained when the condensation was carried out by the general two-stage procedure (overall yield, 44%).

A corresponding reaction between neryltriphenylphosphonium bromide (3.34 m mole) and the all-*E*-aldehyde (1.22 m mole) gave the *Z*-6, *Z*-18-nonaene (77%), λ_{max} ($CHCl_3$) 295, 302, 347 inf. 369 inf. 388, 411, 437 nm, contaminated with the *Z*-**6**, *Z*-**8**, *Z*-**16**, *Z*-**18**-isomer (*ca* 45%), τ 7.96(C-10-Me and C-15-Me), 8.17 (C-6-Me and C-19-Me), 8.30 (C-2-Me and C-23-Me), 8.37 (C-2'-Me and C-23'-Me), δ 17.08 (C-10-Me and C-15-Me), 17.66 (C-2-Me and C-23-Me), 24.50 (C-6-Me and C-19-Me), 25.73 (C-2'-Me and C-23'-Me), 26.90 (C-4 and C-21), 32.22 (C-5 and C-20) ppm.

(c) By the general one-stage procedure, the *Z*-phosphine oxide (4 m mole) and the all-*E*-dial **29** (2 m mole) gave the *Z*-10-hexaenal **30** (33%), λ_{max} ($CHCl_3$) 392 inf., 407 nm (with no significant change in intensity or wavelength of absorption on iodine-catalysed equilibration), ν_{max} (film) 2740, 1675, 1660, 1635, 1615, 1570, 995, 965, 855, 840, 690 cm^{-1}, τ 0.57 (CHO), 2.83–4.08 (m, olefinic protons), 4.87 (C-14-H), 7.78–7.83 (m, CH_2CH_2), 7.97 (C-7-Me), 8.09 (C-2-Me and C-11-Me), 8.29 (C-15-Me), 8.36 (C-15-Me), δ 9.53 (C-2-Me), 13.04 (C-7-Me), 17.66 (C-15-Me), 24.27 (C-11-Me), 25.67 (C-15-Me), 26.90 (C-13), 32.86 (C-12), 194.20 (C-1), ppm; *m/e* 284 (100%, M), 215 (53%, M-C_5H_9), (Found: M^+, 284.2157. $C_{20}H_{28}O$ requires: *M*, 284.2140) contaminated with the all-*E*-hexaenal (*ca* 30%).

(d) Wittig reaction between geranyltriphenylphosphonium bromide (5.2 m mole) and the all-*E*-dial **29** (5.2 mole) using n-BuLi as base, followed by chromatography in benzene gave: (i) the *Z*-**8**-hexaenal (30%) as a very viscous red-coloured oil λ_{max} ($CHCl_3$) 405 nm (I_2-catalysed equilibration produced a significant increase in both λ and ε), τ 0.58 (CHO), 2.86–4.19 (m, olefinic protons), 4.88 (br, C-14-H), 7.83–7.86 (m, CH_2CH_2), 7.88 (C-7-Me), 8.12 (C-11-Me), 8.18 (C-2-Me), 8.29 (C-15-Me), 8.36 (C-15-Me). *m/e* 284 (100%, M), 215 (71%, M-C_5H_9), (Found: M^+, 284.2141. $C_{20}H_{28}O$ requires: *M*, 284.2140), and (ii) the all-*E*-hexaenal **31** (70% of the total of hexaenals), as red-orange oil, λ_{max} ($CHCl_3$), 341 inf., 362 inf., 383 inf., 407 nm, λ_{max} (n-hexane) 267 inf., 272, 332 inf., 352 inf., 367, 384, 406 nm (ε 5100, 5600, 19900, 33800, 47500, 58400, 52000) (iodine-catalysed equilibration produced no significant change in the intensity or wavelength of absorption), ν_{max} (film) 2740, 1675, 1660, 1635, 1615, 1570, 995, 965, 860, 845, 690 cm^{-1}, τ 0.58 (CHO), 2.87–4.08 (7H, m, olefinic protons), 4.86 (br, C-14-H), 7.81–7.84 (m, CH_2CH_2), 7.96 (C-7-Me), 8.09 (C-11-Me), 8.13 (C-2-Me), 8.29 (C-15-Me), 8.36 (C-15-Me), δ 9.53 (C-2-Me), 13.04 (C-7-Me), 17.08 (C-11-Me), 17.66 (C-15-Me), 25.67 (C-15-Me), 26.67 (C-13), 40.29 (C-12), 123.80, 125.61, 126.84, 127.72, 128.53, 130.05, 131.69, 134.50, 136.55, 137.83, 141.75, 148.94, 194.12 (C-1), ppm *m/e* 284 (85%, M), 215 (100%, M-C_5H_9), (Found: M^+, 284.2121. $C_{20}H_{28}O$ requires: *M*, 284.2140).

(e) By the general one-stage procedure, the *Z*-phosphine oxide (1.27 m mole) and all-*E*-2,7,11,15-tetramethylhexadeca-2,4,6,8,10,14-hexaen-1-al **31**, (0.63 m mole) gave the *Z*-6-nonaene **32** (70%), λ_{max} 273 inf. 284, 295, 340 inf. 361 inf. 379, 401, 426 nm, ν_{max} (KBr) 1635, 1590, 965, 895, 835 cm^{-1}, τ 3.33–4.09 (m, olefinic protons) 4.85 (br, C-3-H and C-22-H), 7.80–7.88 (m, CH_2CH_2), 8.05 (C-10-Me and C-15-Me), 8.17 (C-6-Me and C-19-Me), 8.30 (C-2-Me and C-23-Me), 8.37 (C-2-Me and C-23-Me), δ 12.81 (C-10-Me and C-15-Me), 16.96 (C-19-Me), 17.66 (C-2-Me and C-23-Me), 24.15 (C-6-Me), 25.67 (C-2-Me and C-23-Me), 26.72

(C-21), 26.90 (C-4), 32.81 (C-5), 40.23 (C-20) ppm [*m/e* 404 (100%, M), 335 (17%, M-C_5H_9), (Found: M^+ 404.3466. Calc. for $C_{30}H_{44}$, *M* 404.3443] contaminated with the all-*E*-nonaene (*ca.* 25%).

All-*E*-3, 7, 11-*trimethyldodeca*-2, 6, 10-*trienyldiphenylphosphine oxide* (**26**)

The phosphine oxide was prepared from a 3:2 mixture of all-*E* and *Z*-2, *E*-6-isomers of farnesol, in an identical manner to that described for the preparation of *Z*-(3,7-dimethylocta-2,6-dienyl)diphenylphosphine oxide (**4**) from nerol.

Chlorination of a 3:2 mixture of all-*E* and *Z*-2, *E*-6-isomers of farnesol led (73%) to a 3:2 mixture of all-*E* and *Z*-2, *E*-6-isomers of 1-chloro-3,7,11-trimethyldodeca-2,6,10-triene as a colourless liquid, ν_{max} (film) 1660, 845 cm^{-1}, τ 4.55 (t, *J* 8, C-2-H), 4.90 (br, C-6-H, C-10-H), 5.91 (d, *J* 8, C-1-H), 7.84-7.96 (m, CH_2CH_2), (C-3-Me of *Z*-2, *E*-6-isomer), 8.26 (C-3-Me of all-*E*-isomer), 8.30 (C-11-Me-*E*), 8.38 (C-7-Me, C-11-Me-*Z*).

Reaction with lithium diphenylphosphide, followed by oxidation and chromatography on silica gel impregnated with 20% $HgNO_3$, using EtOAc as eluant gave:

(i) the all-*E*-phosphine oxide (34%, eluted second) which crystallised from n-hexane as colourless needles, m.p. 79–80°, ν_{max} (KBr) 855, 770, 745, 720, 695 cm^{-1}, τ 2.26–2.73 (m, PPh_2), 4.81 (apparent q, *J* 7, C-2-H), 5.01 (br, C-6-H, C-10-H), 6.95 (dd, *J* 15 and 8, C-1-H), 8.02 (br, CH_2CH_2), 8.34 (C-11-Me-*E*), 8.42 and 8.44 (C-7-Me and C-11-Me-*Z*), 8.54 (d *J* 2, C-3-Me), δ 15.96 (C-7-Me), 16.37 (C-3-Me), 17.66 (C-11-Me-*Z*), 25.73 (C-11-Me-*E*), 26.49 (C-5), 26.72 (C-9), 30.85 (C-1, d, J_{CP} 69), 39.71 (C-4, C-8), 112.10, 112.45, 123.80; 124.32, 128.18, 128.65, 130.87, 131.17, 131.63, 134.85, 135.08, 140.81, 141.28 ppm [*m/e* 406 (29%, M), 337 (35%, M-C_6H_9), 269 (24%, M-$C_{10}H_{17}$), 202 (100%), 201 (84%, $POPh_2$)], (Found: C, 79.9; H, 8.9. M^+, 406.2440. $C_{27}H_{35}OP$ requires: C, 79.8; H, 8.7%. *M*, 406.2425).

(ii) The *Z*-2, *E*-6-phosphine oxide (18%, eluted first) which crystallised from hexane as colourless needles, m.p. 78–80° and mixed m.p. 62–69° with the all-*E*-isomer, ν_{max} (KBr) 850, 745, 720, 695 cm^{-1}, τ 2.25–2.71 (m, PPh_2), 4.81 (apparent q, *J* 7, C-2-H), 4.99 (br, C-6-H, C-10-H), 6.94 (dd, *J* 15 and 8, C-1-H), 8.0–8.1 (m, CH_2CH_2), 8.34 (C-11-Me-*E* and C-3-Me), 8.42 (C-7-Me and C-11-Me-*Z*), δ 16.02 (C-7-Me), 17.66 (C-11-Me-*Z*), 23.39 (C-3-Me), 25.67 (C-11-Me-*E*), 25.96 (C-5), 26.67 (C-9), 30.56 (C-1, d, J_{CP} 72), 31.99 (C-4), 39.65 (C-8), 112.57, 112.92, 123.74, 124.27, 128.18, 128.65, 130.70, 131.05, 131.52, 134.97, 135.20, 140.70, 141.17 ppm., [*m/e* 406 (90%, M), 337 (96%, M-C_6H_9), 269 (100%, M-$C_{10}H_{17}$), 202 (98%), 201 (98%, $POPh_2$)], (Found: C, 79.5; H, 8.9%; M^+ 406.2446).

(*Z*-6) 3,7,11-*Trimethyldodeca*-2,4,6,10-*tetraenal* (**25**)

Reduction of methyl (*Z*-6) 3,7,11-trimethyldodeca-2,4,6,10-tetraenoate (**21**) with LAH in dry ether, in usual way, led to (*Z*-6)3,7,11-trimethyldodeca-2,4,6,10-tetraenol (95%) as a colourless viscous oil, λ_{max} (n-hexane) 262 inf. 273 inf, 281, 291 inf. nm (ϵ 18600, 27300, 32200, 25200), ν_{max} (film) 3340, 1630, 960, 835 cm^{-1}, τ 3.57 (dd, *J* 15 and 11, C-5-H), 3.92 (d, *J* 15, C-4-H), 4.15 (d, *J* (11, C-6-H), 4.42 (t, *J* 7, C-2-H), 4.90 (br, C-10-H), 5.80 (d, *J* 7, C-1-H), 7.11 (br, OH), 7.84 and 7.89 (m, CH_2CH_2), 8.18 (C-3-Me and C-7-Me), 8.32 (C-11-Me-*E*), 8.39 (C-11-Me-*Z*), δ 12.51 (C-3-Me), 17.60 (C-11-Me-*Z*), 23.98 (C-7-Me), 25.67 (C-11-Me-*E*), 26.84 (C-9), 32.69 (C-8), 59.12 (C-1), ppm. *m/e* 220 (20%, M), 202 (4%, M-H_2O), 151 (6%, M-C_5H_9), 107 (100%), (Found: M^+, 220.1818. $C_{15}H_{24}O$ requires: *M*, 220.1827).

Oxidation of the tetraenol with MnO_2 in light petroleum (b.p. 40–60°), in the usual way, gave the *Z*-6-tetraenal (74%) as a yellow oil, λ_{max} (n-hexane) 292 inf. 305 inf. 320, 335 nm (ϵ 9400, 17100, 28100, 25900), ν_{max} (film) 2780, 2730, 1660, 1635, 1600, 1570, 960, 890, 830 cm^{-1}, τ 0.04 (d, *J* 8, CHO), 3.08 (dd, *J* 15 and 11, C-5-H), 3.84 (d, *J* 15, *C*-4-*H*), 4.03 (d, *J* 11, C-6-H), 4.11 (d, *J* 8, C-2-H), 4.93 (br, C-10-H), 7.72 (C-3-Me), 7.7–7.9 (m, 4H), 8.12 (C-7-Me), 8.31 (C-11-Me-*E*), 8.38 (C-11-Me-*Z*), δ 12.92 (C-3-Me), 17.60 (C-11-Me-*Z*), 24.33 (C-7-Me), 25.67 (C-11-Me-*E*), 26.90 (C-9), 32.98 (C-8), 123.56 (C-10), 126.02, 128.65, 132.16, 132.39, 132.63, 145.84, 154.79 (C-3), 190, 52 (C-1) ppm. *m/e* 218 (100%, M), 149 (56%, M-C_5H_9), (Found: M^+, 218.1669. $C_{15}H_{20}$ requires: *M*, 218.1671).

Z-6, *Z*-12 and *Z*-6-*Isomers of* 2,6,10,15,19,23-*hexamethyltetracosa*-2,6,8,10,12,14,18,22-*octaene* (**28**)

By the general two stage procedure, reaction between all-*E*-3,7,11-trimethyldodeca-2,6,10-trienyldiphenylphosphine oxide (0.4 g) and (*Z*-6)3,7,11-trimethyldodeca-2,4,6,10-tetraenal (0.25 g) led to the *erythro*-β-hydroxyphosphine oxide **27** (0.20 g, 32%) as a viscous oil (eluted first), λ_{max} ($CHCl_3$) 269 inf., 280 inf., 289, 300 inf. nm, ν_{max} (film) 3400, 960, 880, 770, 745, 720, 690 cm^{-1}, τ 6.73 (br, t, *J* 9, *CH*$POPh_2$), 8.66 (d, *J* 3, C-15-Me), *m/e* 624 (*M*, not observed), 450 (2%), 406 (0.7%, M-PPh_2O_2H), 297 (51%), 284 (100%), and the *threo*-β-hydroxyphosphine oxide (0.26 g, 42%) as a viscous oil (eluted second), λ_{max} ($CHCl_3$), 269 inf., 279 inf., 290, 300 nm, ν_{max} (film) 3340, 960, 880, 770, 750, 720, 695 cm^{-1}, τ 6.49 (t d, *J* 11 and 8, *CH*$POPh_2$), 8.57 (d, *J* 3, C-15-Me), *m/e* 624 (0.3%, M), 606 (0.2%, M-H_2O), 555 (0.1%, M-C_5H_9), 450 (8%), 406 (87%, M-PPh_2O_2H), 337 (47%, M-PPh_2O_2H-C_5H_9), 297 (100%), 284 (45%), 269 (86%, M-PPh_2O_2H-$C_{10}H_{17}$).

Treatment of the *erythro* β-hydroxyphosphine oxide (0.085 g) with NaH in DMF, according to the general procedure, followed by chromatography using 2% acetone in n-hexane gave the *Z*-6, *Z*-12-octaene **28** (19 mg., 35%) as a pale yellow oil, λ_{max} (n-hexane) 250, 257, 301 inf., 318 inf., 332, 349, 367 nm (ϵ 9900, 10100, 14600, 26300, 45000, 63300, 54500 (with a significant increase in intensity and a slight increase in wavelength of absorption on I_2-catalysed-equilibration), ν_{max} (film), 1635, 960, 885, 830, 775 cm^{-1}, τ 3.34–4.14 (7H, olefinic protons on chromophore), 4.88 (3H, br s, olefinic protons on isolated double bonds), 7.8–7.98 (m, 12H), 8.09 (C-10-Me), 8.18 (C-6-Me), 8.20 (C-15-Me), 8.31 (C-2-Me-*E*, C-23-Me-*E*), 8.38 (C-2-Me-*Z*, C-23-Me-*Z*, C-19-Me), δ 12.40 (C-10-Me), 16.02 (C-19-Me), 16.61 (C-15-Me), 17.60 (C-2-*Me-Z*, C-23-Me-*Z*), 24.09 (C-6-Me), 25.67 (C-2-Me-*E*, C-23-Me-*E*), 26.84 (C-4, C-17, C-21), 32.81 (C-5) 39.77 (C-20), 40.53 (C-16), 120.58, 123.27, 123.86, 124.38, 125.26, 125.79, 126.60, 131.05, 131.69, 135.27, 135.38, 135.67, 139.00, 140.35 ppm, *m/e* 406, (100%, M), 337 (3%, M-C_5H_9), 269 (64%, M-$C_{10}H_{17}$). (Found: M^+, 406.3589. $C_{30}H_{46}$ requires: *M*, 406.3599).

Treatment of the *threo*-β-hydroxyphosphine oxide (0.11 g) with NaH in DMF, according to the general procedure gave the *Z*-6-octaene (38 mg, 53%), as a pale yellow oil, ν_{max} (film) 1630, 960, 880, 830 cm^{-1}, τ 3.47–4.15 (7H, m, olefinic protons on chromophore), 4.87 (3H, br s, olefinic protons on isolated double bonds), 7.8–7.98 (m, 12H), 8.08 (C-10-Me), 8.19 (C-6-Me, C-15-Me), 8.30 (C-2-Me-*E*, C-23-Me-*E*), 8.38 (C-2-Me-*Z*, C-23-Me-*Z*, C-19-Me), δ 12.68 (C-10-Me), 16.02 (C-19-Me), 16.87 (C-15-Me), 17.66 (C-2-Me-*Z*, C-23-Me-*Z*), 24.09 (C-6-Me), 25.66 (C-2-Me-*E*, C-23-Me-*E*), 26.82, (C-4, C-17, C-21), 32.82 (C-5), 39.80 (C-20), 40.29 (C-16), 123.95, 124.13, 124.44, 125.95, 126.74, 127.47, 129.54, 129.78, 131.05, 131.36, 131.72, 134.81, 135.30, 135.54, 138.82, 139.30 ppm. *m/e* 406 (100%, M), 337 (4%, M-C_5H_9), 269 (72%, M-$C_{10}H_{17}$). (Found: M^+, 406.3572).

Acknowledgement—We thank the S.R.C. for a studentship (to J.M.C.) and the Royal Society for an equipment grant.

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