

## Carotenoids and Related Compounds. Part XXX.<sup>1</sup> Stereochemistry and Synthesis of Phytoene

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Studies on models synthesised by stereochemically controlled routes have been used to elucidate the configurations of the central triene chromophores in the phytoenes (7,8,11,12,7',8',11',12'-octahydro- $\psi,\psi$ -carotenes). The common natural phytoene has been shown to be *cis* about the 15,15'-double bond only, and the main phytoene from *Flavobacterium dehydrogenans* to be the all-*trans*-isomer. Both these isomers have been synthesised, and their stereomutation has been studied.

PHYTOENE (7,8,11,12,7',8',11',12'-octahydro- $\psi,\psi$ -carotene) is generally recognised as the first C<sub>40</sub> conjugated polyene in the biosynthesis of carotenoids.<sup>2</sup> Its gross structure (1d) was established by oxidative degradation,<sup>3</sup> and subsequently confirmed by mass spectroscopy<sup>4</sup> and synthesis.<sup>5</sup>

At least two isomers of phytoene occur in nature, though it is not yet known whether both are involved directly in the biosynthesis of other carotenoids or only one.<sup>6</sup> The readily available isomer from carrot oil and tomato paste was assigned a 15-*cis*-configuration since (unlike the perhydro-derivative) it gave no crystalline thiourea adduct.<sup>7</sup> This conclusion was supported by i.r. evidence; a band near 760 cm<sup>-1</sup> may

be attributed to C-H out-of-plane deformation of the disubstituted *cis*-double bond<sup>8</sup> (cf. bands near 780 and 965 cm<sup>-1</sup> for the 15-*cis*- and all-*trans*-isomers respectively of many other carotenoids<sup>8</sup>). In contrast the phytoene isolated from diphenylamine-inhibited cultures of *Flavobacterium dehydrogenans* exhibited a C-H out-of-plane deformation suggesting a 15-*trans*-structure.<sup>4,8,9</sup>

The n.m.r. spectra of both isomers revealed that the four unconjugated, trisubstituted double bonds (at positions 5-, 5'-, 9-, and 9'-) all have the *trans*-configuration.<sup>4,5</sup> The n.m.r. spectra of the main phytoene fractions from *Chlorella vulgaris* (mutant G.77),<sup>5</sup> *Phycomyces blakesleeanus*, *Rhodospirillum rubrum* (diphenylamine-inhibited culture), and commercial tomatoes

<sup>5</sup> J. B. Davis, L. M. Jackman, P. T. Siddons, and B. C. L. Weedon, *J. Chem. Soc. (C)*, 1966, 2154.

<sup>6</sup> B. C. L. Weedon, *Pure Appl. Chem.*, 1973, **35**, 113.

<sup>7</sup> W. J. Rabourn, F. W. Quackenbush, and J. W. Porter, *Arch. Biochem. Biophys.*, 1954, **48**, 267.

<sup>8</sup> B. C. L. Weedon, in 'Carotenoids,' ed. O. Isler, Birkhäuser, Basel, 1971, p. 267.

<sup>9</sup> N. Khatoon, D. E. Loeber, T. P. Toube, and B. C. L. Weedon, *J.C.S. Chem. Comm.*, 1972, 996.

<sup>1</sup> Part XXIX, J. R. Hlubucek, J. Hora, S. W. Russell, T. P. Toube, and B. C. L. Weedon, *J.C.S. Perkin I*, 1974, 848.

<sup>2</sup> T. W. Goodwin, in 'Carotenoids,' ed. O. Isler, Birkhäuser, Basel, 1971, p. 577.

<sup>3</sup> W. J. Rabourn, and F. W. Quackenbush, *Arch. Biochem. Biophys.*, 1956, **61**, 111.

<sup>4</sup> O. B. Weeks, A. G. Andrewes, B. O. Brown, and B. C. L. Weedon, *Nature*, 1969, **224**, 879.

showed that these metabolites have the same configuration as the main isomer from carrot oil; traces of a *trans*-isomer have been detected in most of these sources.<sup>9,10</sup> Significant amounts of a 15-*trans*-phytoene have also been reported in 2-hydroxybiphenyl-inhibited cultures of *R. rubrum* and *Rhodospseudomonas spheroides*,<sup>11</sup> and in fluoren-9-one-inhibited cultures of *Verticillium agaricum*,<sup>12</sup> *R. rubrum*,<sup>13</sup> and *Mucor hiemalis*.<sup>14</sup> It has not yet been established whether all these 'trans-phytoenes,' are identical with the *trans*-isomer from *F. dehydrogenans*.

Prior to the work now reported little information was available on the configuration of the 13- and 13'-double bonds in the phytoenes. Though results on the incorporation of (4*R*)-[2-<sup>14</sup>C,4-<sup>3</sup>H]mevalonic acid were consistent with a *trans*-formulation about these bonds, the evidence was not conclusive.<sup>8,15</sup> Our investigations were undertaken to resolve unambiguously the uncertainty regarding the stereochemistry of the central triene unit in the common *cis*-phytoene, and in its *trans*-isomer from *F. dehydrogenans* (for preliminary publications see refs. 6 and 9). By <sup>1</sup>H and <sup>13</sup>C n.m.r. studies Granger *et al.*<sup>16</sup> have independently come to the same conclusions regarding the main *cis*- and *trans*-phytoenes from inhibited cultures of *R. rubrum* and *Mucor hiemalis*.

Pentan-2-one (2a) was converted into a mixture of the esters (3a) and (4a) by means of a Horner reaction with methoxycarbonylmethyl diethyl phosphonate. The esters were separated by preparative g.l.c. Their configurations, like those of the  $\alpha\beta$ -unsaturated esters and aldehydes mentioned below, were assigned unequivocally by the chemical shifts of the  $\beta$ -methyl protons in the n.m.r. spectra.<sup>17</sup> Reaction of the *trans*-ester (3a) with lithium aluminium hydride in ether gave the *trans*-alcohol; such reductions of  $\alpha\beta$ -unsaturated esters are known to occur with retention of configuration.<sup>17</sup> Oxidation of the alcohol to yield the corresponding *trans*-aldehyde (6a) was performed either with active manganese dioxide (53% yield) or with Fetizon's reagent (88%); again retention of stereochemistry was observed. Treatment of the *trans*-alcohol with triphenylphosphonium bromide produced the *trans*-Wittig salt (5a).

A similar sequence of reactions starting from the *cis*-ester (4a) gave the *cis*-alcohol and thence the *cis*-aldehyde (7a), although the yield of the latter was lower than in the isomeric series. The preparation of the Wittig salt, however, resulted in the production of both the *cis*- and the *trans*-isomers as expected.<sup>18</sup> Accord-

ingly, the reaction with triphenylphosphonium bromide was carried out on a mixture of the *cis*- and *trans*-alcohols and the product was fractionally crystallised: the first crop of crystals was the pure *trans*-salt; the third crop contained a greatly enhanced amount of the *cis*-compound.

It has previously been shown that there is retention of configuration during Wittig condensations with  $\beta$ -methyl  $\alpha\beta$ -unsaturated aldehydes and  $\beta$ -methyl allylic phosphonium salts; under most conditions the newly formed double bond consists of a mixture of *cis*- and *trans*-forms which may be distinguished by the C-H out-of-plane deformation absorptions in the i.r. spectra or by n.m.r.<sup>18,19</sup> These general conclusions were confirmed in the present work by the isolation of four stereoisomers of the model triene (1a). Condensations between the *trans*-aldehyde (6a) and the *trans*-Wittig salt either in 1,2-epoxybutane<sup>20</sup> or with potassium hydroxide in propan-2-ol<sup>21</sup> gave mixtures of the *trans,trans,trans*- (8a) and *trans,cis,trans*- (9a) trienes. Preparative g.l.c. yielded the separate isomers.

The corresponding condensations between the *cis*-aldehyde (7a) and the *trans*-phosphonium salt (5a) yielded the *trans,trans,cis*- (10a) and *trans,cis,cis*- (11a) isomers. The compounds were separated by t.l.c. on silver nitrate-impregnated silica gel plates.

Attempts to prepare the *cis,cis,cis*- and *cis,trans,cis*-isomers by condensing the *cis*-aldehyde (7a) with the partially purified *cis*-Wittig salt were accompanied by stereomutation of the phosphonium compound and only traces of materials presumed to be the desired products were detected in the reaction mixture.

6-Methylheptan-2-one<sup>22</sup> (2b) was converted into a mixture of the esters (3b) and (4b) by the same procedure as used in the previous series, and the isomers were again separated by g.l.c. Reduction of each ester gave the corresponding alcohol, which could be converted in high yield into the aldehyde [(6b) and (7b), respectively] by oxidation with Fetizon's reagent. Use of other oxidising agents gave lower yields (manganese dioxide) or produced mixtures of the two stereoisomers (dichlorodicyanobenzoquinone). The *trans*-Wittig salt (5b) was prepared from the *trans*-alcohol in the usual manner. We were unable to obtain the *cis*-Wittig salt from the reaction involving the *cis*-alcohol.

The Wittig condensation between the salt (5b) and the *trans*-aldehyde (6b) yielded a mixture of the *trans,cis,trans*- (9b) and the all-*trans*-triene (8b). These isomers could not be separated with retention of stereochemistry. The *trans,trans,cis*- (10b) and *trans,cis,cis*-

<sup>10</sup> Aung, Than, P. M. Bramley, B. H. Davies, and A. F. Rees, *Phytochem.*, 1972, **11**, 3187.

<sup>11</sup> B. Maudinas, R. Herber, J. Villoutreix, and P. Granger, *Biochimie*, 1972, **54**, 1085.

<sup>12</sup> L. R. G. Valadon, R. Herber, J. Villoutreix, and B. Maudinas, *Phytochem.*, 1973, **12**, 161.

<sup>13</sup> B. Maudinas, R. Herber, and J. Villoutreix, *Photochem. Photobiol.*, 1972, **16**, 515.

<sup>14</sup> R. Herber, B. Maudinas, J. Villoutreix, and P. Granger, *Biochim. Biophys. Acta*, 1972, **270**, 194.

<sup>15</sup> T. W. Goodwin, *Pure Appl. Chem.*, 1969, **20**, 483.

<sup>16</sup> P. Granger, B. Maudinas, R. Herber, and J. Villoutreix, *J. Magnetic Resonance*, 1973, **10**, 43.

<sup>17</sup> J. W. K. Burrell, R. F. Garwood, L. M. Jackman, E. Oskay, and B. C. L. Weedon, *J. Chem. Soc. (C)*, 1966, 2144.

<sup>18</sup> G. Pattenden and B. C. L. Weedon, *J. Chem. Soc. (C)*, 1968, 1984.

<sup>19</sup> G. Pattenden and B. C. L. Weedon, *J. Chem. Soc. (C)*, 1968, 1997.

<sup>20</sup> Cf. D. E. Loeber, S. W. Russell, T. P. Toubé, B. C. L. Weedon, and J. Diment, *J. Chem. Soc. (C)*, 1971, 404.

<sup>21</sup> G. M. Leeder, personal communication.

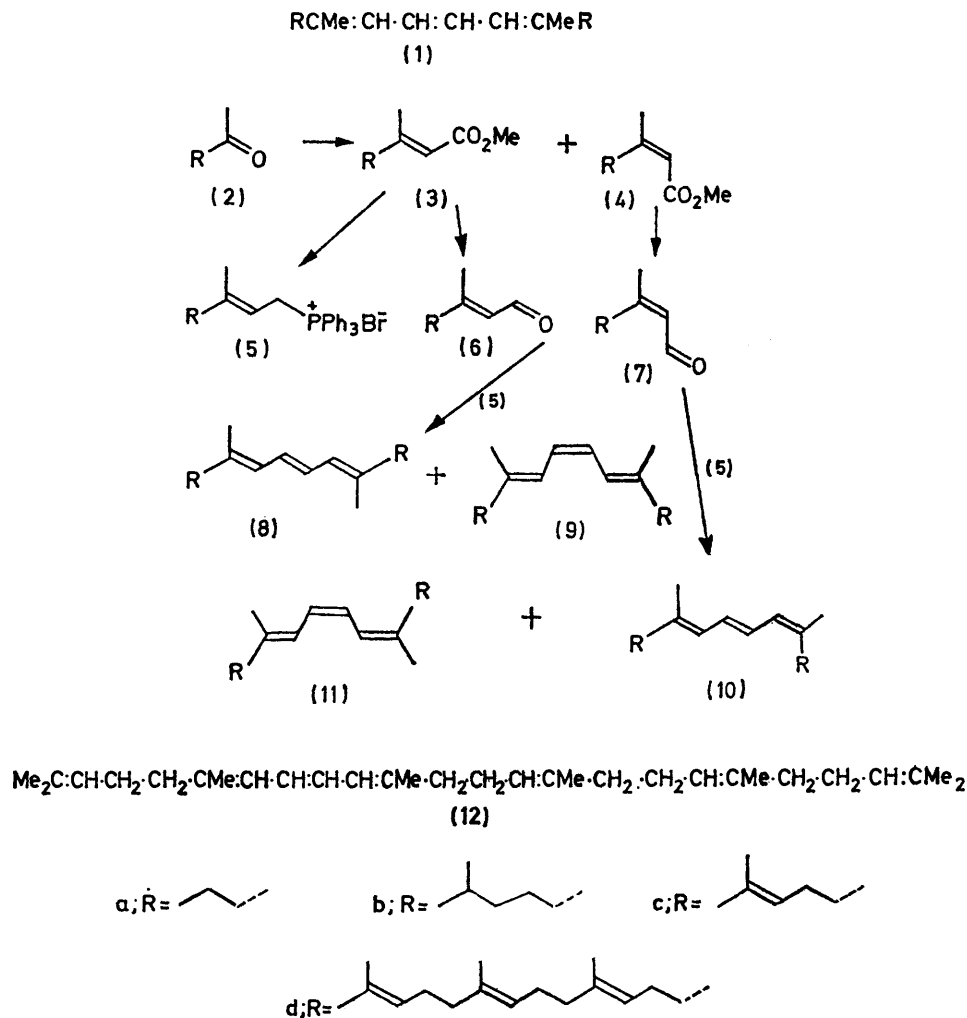
<sup>22</sup> W. Kimel, N. W. Sax, K. Kaiser, G. G. Eichmann, G. O. Chase, and A. Ofner, *J. Org. Chem.*, 1958, **23**, 153.

(11b) compounds were prepared in an analogous manner from the same Wittig salt (5b) and the *cis*-aldehyde (7b).

The *trans*- (3d) and *cis*- (4d) esters were elaborated in the usual way<sup>5</sup> from (*trans,trans*-)farnesylacetone, and separated by preparative t.l.c.; each was converted as before into the corresponding aldehyde, *viz.* *trans*- (6d) and *cis*-geranylaldehyde (7d).<sup>5</sup> Condensation of (*trans*-)geranylgeranyltriphenylphosphonium bromide<sup>5</sup> (5d)

isomeric hydrocarbons (1c). The preparation of a mixture of all four isomers has previously been reported.<sup>5</sup> The C<sub>30</sub> model (12) was produced by the reaction of *trans*-citral (6c) with geranylgeranyltriphenylphosphonium bromide<sup>5</sup> (5d).

Computation (from the 220 MHz n.m.r. spectra) of the coupling constants for the AA'BB' system of the olefinic protons of the triene units for the all-*trans*- (8a)



with *trans*-geranylaldehyde (6d) yielded a mixture of 15-*cis*- (9d) and all-*trans*-phytoene (8d), which was separated by column chromatography on alumina.<sup>10,23</sup> A mixture of the *trans,trans,cis*- (10d) and *trans,cis,cis*- (11d) isomers was prepared in an analogous manner from *cis*-geranylaldehyde (7d). All condensations with the geranylgeranyl reagent (5d) gave products consisting largely (*ca.* 80%) of the isomer with the *trans*-configuration about the newly formed double bond. In the other Wittig reactions described *cis*-olefination predominated.

The condensation of the (*trans*-)geranyl Wittig reagent<sup>5</sup> (5c) with *cis*- (7c) and *trans*-citral (6c), respectively, gave the corresponding mixtures of pairs of

and *trans,cis,trans*- (9a) model compounds (see Table 1) shows that the spin-spin splitting between the protons on

TABLE 1

Coupling constants (Hz) of olefinic protons in conjugated trienes RCMe:CH<sub>B</sub>:CH<sub>A</sub>:CH<sub>A'</sub>:CH<sub>B'</sub>:CMeR

	$J_{AB}$	$J_{AB'}$	$J_{AA'}$	$J_{BB'}$
(8a)	11.0	-1.1	14.6	0.1
(9a)	11.5	-1.4	10.8	-0.2
Phytoene	12.0	-1.3	10.6	-0.3

the central double bond is 14.6 Hz in the *trans*-case and 10.8 Hz in that of the *cis*-isomer. The latter has coupling constants in very good agreement with those

<sup>23</sup> F. B. Jungalwala and J. W. Porter, *Arch. Biochem. Biophys.*, 1964, **48**, 267.

computed for the common natural *cis*-phytoene (9d) (see Table 1); in particular, the value of 10.6 Hz for  $J_{15,15'}$  in the natural carotenoid confirms the central *cis*-assignment of its stereochemistry. All the models having a central *cis*-bond exhibit an i.r. absorption band at 758—772  $\text{cm}^{-1}$  whereas in those with the central *trans*-configuration the corresponding deformation band lies in the range 950—968  $\text{cm}^{-1}$ ; the main phytoene from carrot oil and most other natural sources has the *cis*-absorption (763  $\text{cm}^{-1}$ ) only, whereas that from *F. dehydrogenans* has the *trans*-absorption (958  $\text{cm}^{-1}$ ).

The spectra of these compounds (Table 2) provide further evidence for an unambiguous assignment of the stereochemistry about the triene unit in phytoene.

TABLE 2  
Selected spectroscopic data for synthetic trienes

	$\nu_{\text{max.}}$ / $\text{cm}^{-1}$	$\lambda_{\text{max.}}$ (hexane)/nm	$\delta$ (100 MHz; $\text{CCl}_4$ )
<i>trans,trans,trans</i>			
(8a)	965	273.5, 283.5, 296	1.72, 1.72
(8b) †	958	273.5, 284, 296	1.72, 1.72
(8c) †	968	275.5, 285.5, 297.5	1.74, 1.74
(8d)	950	275, 286, 298	1.75, 1.75
<i>trans,cis,trans</i>			
(9a)	766	273.5, 283.5, 296	1.72, 1.72
(9b) †	765	273.5, 284, 296	1.72, 1.72
(9c) †	770	275.5, 285.5, 297.5	1.74, 1.74
(9d)	758	276, 286, 298	1.73, 1.73
<i>trans,trans,cis</i>			
(10a)	956	272.5, 283, 295.5	1.72, 1.76
(10b) †	965	273, 283.5, 296	1.72, 1.75
(10c) †	965	275.5, 285.5, 297.5	1.74, 1.78
(10d) †	960	275.5, 285.5, 298	1.74, 1.77
<i>trans,cis,cis</i>			
(11a)	758	272.5, 282.5, 295	1.72, 1.80
(11b) †	772	273, 283.5, 296	1.72, 1.80
(11c) †	772	275.5, 285.5, 297.5	1.74, 1.81
(11d) †	766	275.5, 285.5, 298	1.74, 1.82
(12)	960, 768	275.5, 286, 298	1.74, 1.74

† From mixtures of (8) and (9). ‡ From mixtures of (10) and (11).

The u.v. spectra of the compounds with unconjugated double bonds  $\gamma\delta$  to the triene unit (series c and d) have maxima exhibiting a bathochromic shift of 1.5—3 nm relative to those compounds without such isolated double bonds. We ascribe this effect to non-bonded  $\pi$ - $\pi$  interaction between the remote bond and the triene chromophore which can occur by coiling of the alkyl chain. This long range effect is also seen in the n.m.r. spectra, the chemical shifts of the methyl groups about the triene unit in the a and b series being 0.01—0.03 p.p.m. further upfield than those of the corresponding isomers in the other series. The shift of a methyl group attached to a *trans*-double bond of the triene is independent of the stereochemistry of the rest of the chromophore; a methyl group on a *cis*-trisubstituted olefinic bond resonates 0.02—0.04 p.p.m. further downfield if the adjacent conjugated double bond is *trans* and 0.07—0.08 p.p.m. if it is *cis*. In the common natural (*cis*-)phytoene this absorption is at  $\delta$  1.74 for both 13- and 13'-methyls. Accordingly, the configuration of the natural carotenoid

is established as *trans,cis,trans* (9d). The same evidence establishes the all-*trans*- (8d) stereochemistry for the phytoene isomer ( $\delta$  1.73) from *F. dehydrogenans*.

The *cis*-configuration of the common natural phytoene is surprisingly stable. However Jungalwala and Porter<sup>23</sup> found that stereomutation occurs on irradiation with light in the presence of iodine to give a product which appeared to consist mainly of the all-*trans*-isomer. We have now examined such products by 220 MHz n.m.r. spectroscopy. In addition to the all-*trans*-isomer, ca. 10% of the *trans,trans,cis*- (together with, possibly, the *cis,trans,cis*-) and ca. 25% of the *trans,cis,cis*- (together with *cis,cis,cis*-) isomers are also formed; the unconjugated double bonds are unaffected. In similar stereomutations of the all-*trans*-phytoene, ca. 25% of the product consists of isomers with a *cis*-configuration about the 13- and/or 13'-double bond. Granger *et al.*<sup>16</sup> have detected the 13-*cis*-isomer in the phytoene from inhibited cultures of *R. rubrum* and *Mucor hiemalis*.

#### EXPERIMENTAL

All operations were carried out in an inert atmosphere whenever possible. Light petroleum refers to the fraction of b.p. 40—60°.

Except where indicated to the contrary, i.r. spectra were determined for liquid films (selected bands only are quoted), n.m.r. spectra for solutions in carbon tetrachloride at 100 MHz, and u.v. spectra for solutions in hexane. Mass spectra were recorded on an A.E.I. MS902 instrument; selected lines only are quoted.

*cis*- and *trans*-Methyl 3-Methylhex-2-enoate (4a) and (3a).—Solutions of pentan-2-one (17.5 g) in dry ether (200 ml), and methanolic sodium methoxide [from sodium (7 g) in dry methanol (200 ml)] were added simultaneously but separately to a stirred solution of methoxycarbonylmethyl diethyl phosphonate<sup>24</sup> (46 g) in dry ether (200 ml) over 30 min. The mixture was then stirred for a further 30 min, poured into water, and extracted with ether (3 × 100 ml). The combined extracts were washed with water, dried, and evaporated. Distillation of the residue gave a mixture of the *cis*- and *trans*-esters (24.6 g, 78%) as a liquid, b.p. 65° at 15 mmHg;  $\nu_{\text{max.}}$  1715, 1650, 1448, and 1225  $\text{cm}^{-1}$ . The *cis*- and *trans*-esters were separated by g.l.c. (20% polyethylene glycol adipate column at 65°) to give: (i) the *cis*-ester,  $\lambda_{\text{max.}}$  220 nm ( $\epsilon$  10,500);  $\nu_{\text{max.}}$  1723, 1645, 1440, and 1215  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.94 (3H, t,  $J$  6.5 Hz), 1.13—1.75 (2H, m), 1.87 (3H, d,  $J$  1.5 Hz), 2.67br (2H, t,  $J$  8 Hz), 3.67 (3H, s), and 5.65br (1H, s) [Found:  $M^+$ , 142.100 (100%).  $\text{C}_8\text{H}_{14}\text{O}_2$  requires  $M$ , 142.099], and (ii) the *trans*-ester,  $\lambda_{\text{max.}}$  (hexane) 221 nm ( $\epsilon$  14,400);  $\nu_{\text{max.}}$  1720, 1650, 1440, and 1220  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.91 (3H, t,  $J$  6.5 Hz), 1.17—2.33 (4H, m), 2.14 (3H, d,  $J$  1.5 Hz), 3.69 (3H, s), and 5.65 (1H, m) (Found:  $M^+$ , 142.099);  $m/e$  142 (95%) and 111 (100%).

*cis*- and *trans*-3-Methylhex-2-en-1-ol.—(i) Lithium aluminium hydride (400 mg) was added in small portions to a stirred solution of the *trans*-ester (2 g) in dry ether (75 ml) over 5 min. The mixture was stirred for 1 h and moist ether (100 ml) was added. A saturated solution of ammonium chloride (5 ml) was then added, the ether layer was separated, and the aqueous layer was extracted with

<sup>24</sup> P. Nyler, *Ber.*, 1924, 57, 1023.

ether (3 × 100 ml). The combined extracts were dried and evaporated. Distillation of the residue gave the *trans*-alcohol (1.7 g, 85%) as a liquid, b.p. 72° at 12 mmHg;  $\nu_{\max}$  3368, 1670, 1475, and 1010  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.90 (3H, t,  $J$  6.5 Hz), 1.08—2.25 (4H, m), 1.34 (1H, s, exchanges with  $\text{D}_2\text{O}$ ), 1.68 (3H, s), 4.16 (2H, d,  $J$  7 Hz), and 5.14 (1H, t,  $J$  6.5 Hz) (Found:  $M^+$ , 114.105.  $\text{C}_7\text{H}_{14}\text{O}$  requires  $M$ , 114.104);  $m/e$  114 (15%) and 71 (100).

(ii) A similar reduction and work-up of the *cis*-ester yielded the *cis*-alcohol (85%); b.p. 43—45° at 12 mmHg;  $\nu_{\max}$  3380, 1665, and 1005  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.90 (3H, t,  $J$  6.5 Hz), 1.1—2.27 (4H, m), 1.73 (3H, d,  $J$  1.5 Hz), 2.24 (1H, s, exchanges with  $\text{D}_2\text{O}$ ), 4.11 (2H, d,  $J$  7 Hz), and 5.95 (1H, t,  $J$  7 Hz) (Found:  $M^+$ , 114.105).

*cis*- and *trans*-3-Methylhex-2-enal (7a) and (6a).—

(i) Traces of moisture were removed from a suspension of Fetizon's reagent<sup>25,26</sup> [silver carbonate—Celite (8 g)] in benzene (100 ml) by azeotropic distillation. The mixture was cooled, the *trans*-alcohol (800 mg) in benzene (10 ml) added, and the mixture boiled for 1 h. The product was cooled, filtered, and evaporated. Distillation of the residual liquid afforded the *trans*-aldehyde (700 mg, 88%) as a liquid, b.p. 63° at 9 mmHg;  $\lambda_{\max}$  230 nm ( $\epsilon$  14,100);  $\nu_{\max}$  2738 and 1678  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.93 (3H, t,  $J$  6.5 Hz), 1.20—2.41 (4H, m), 2.16 (3H, d,  $J$  1.5 Hz), 5.87 (1H, dq,  $J$  8 and 1 Hz), and 9.98 (1H, d,  $J$  7 Hz); 2,4-dinitrophenylhydrazone, m.p. 173—174° (from ethanol) (Found:  $M^+$ , 292.117.  $\text{C}_{13}\text{H}_{18}\text{N}_4\text{O}_4$  requires  $M$ , 292.117).

(ii) An analogous oxidation and work-up of the *cis*-alcohol afforded the *cis*-aldehyde (74.5%); b.p. 55—60° at 13 mmHg;  $\lambda_{\max}$  230 nm ( $\epsilon$  11,500);  $\nu_{\max}$  2760, 1675, and 1630  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.97 (3H, t,  $J$  7.5 Hz), 1.15—2.83 (4H, m), 1.98 (3H, d,  $J$  1.5 Hz), 5.90 (1H, d,  $J$  8 Hz), and 9.96 (1H, d,  $J$  8 Hz); 2,4-dinitrophenylhydrazone, m.p. 180—181° (from ethanol) (Found:  $M^+$ , 292.117).

*trans*-3-Methylhex-2-enyltriphenylphosphonium Bromide (5a).—A mixture of *trans*-3-methylhex-2-en-1-ol (2 g) and triphenylphosphonium bromide (5.6 g) in dry methanol (100 ml) was stirred at 20° for 3 days. The mixture was evaporated and the residue crystallised from chloroform and ethyl acetate to give the product (2.5 g, 50%), m.p. 180—182°. Recrystallisation of a small sample gave the *phosphonium bromide*, m.p. 191°;  $\delta$  ( $\text{CDCl}_3$ ) 0.77 (3H, t,  $J$  6.5 Hz), 0.95—2.18 (4H, m), 1.37 (3H, d,  $J$  4 Hz), 4.5 (2H, dd,  $J$  14 and 8 Hz), 5.1br (1H, t,  $J$  6 Hz), and 7.23 (15H, m) (Found: C, 68.45; H, 6.3; Br, 18.55.  $\text{C}_{25}\text{H}_{28}\text{BrP}$  requires C, 68.5; H, 6.4; Br, 18.25%).

*trans*,*cis*,*trans*- and *trans*,*trans*,*trans*-4,9-Dimethyldodeca-4,6,8-triene (9a) and (8a).—(a) A mixture of *trans*-3-methylhex-2-enal (500 mg, 4.5 mmol), *trans*-3-methylhex-2-enyltriphenylphosphonium bromide (2.5 g, 5.7 mmol), and 1,2-epoxybutane (1 ml) was heated in a sealed tube at 100 °C for 13 h. The product was cooled, dissolved in the minimum volume of chloroform, and chromatographed on a column (alumina grade IV; light petroleum). Distillation (short-path) of the major product gave a mixture of isomers of the triene hydrocarbon (845 mg, 81%) as an oily liquid, b.p. 96° at 0.04 mmHg;  $\lambda_{\max}$  273, 284, and 296 nm;  $\nu_{\max}$  1635, 960, and 767  $\text{cm}^{-1}$ ; preparative g.l.c. (20% diethylene glycol succinate; 115°) gave: (i) the *trans*,*cis*,*trans*-hydrocarbon as an oil,  $\lambda_{\max}$  273.5, 283.5, and 296 nm (relative intensities 83 : 100 : 69);  $\nu_{\max}$  1640 and 770  $\text{cm}^{-1}$ ;  $\delta$  0.90 (6H, t,  $J$  7 Hz), 1.15—1.98 (4H, m), 1.72

(6H, s), 2.06br (4H, t,  $J$  8 Hz), and 5.58—6.24 (4H, m) [Found:  $M^+$ , 192.188 (100%).  $\text{C}_{14}\text{H}_{24}$  requires  $M$ , 192.188]; and (ii) the *trans*,*trans*,*trans*-triene as an oily liquid,  $\lambda_{\max}$  273.5, 283.5, and 296 nm (relative intensities 63 : 100 : 65);  $\nu_{\max}$  1638 and 965  $\text{cm}^{-1}$ ;  $\delta$  0.82 (6H, t,  $J$  7.5 Hz), 1.19—1.65 (4H, m), 1.72 (6H, s), 2.02br (4H, t,  $J$  7.5 Hz), and 5.6—6.25 (4H, m) [Found:  $M^+$  192.188 (100%)]. The ratio of (8a) to (9a) was 2 : 3.

(b) A solution of the *trans*-aldehyde (82 mg, 0.73 mmol) in propan-2-ol (3 ml) was added dropwise to a stirred suspension of the *trans*-Wittig salt (370 mg, 0.84 mmol) in propan-2-ol (7 ml) at −30 °C. The mixture was allowed to warm to −20 °C, aqueous potassium hydroxide solution (4%; 0.2 ml) was added over 5 min, and the mixture was stirred for 30 min at the same temperature and then at 20 °C for 1 h, poured into water (20 ml), and extracted with ether (3 × 20 ml). The combined extracts were washed with water and dried. Evaporation followed by column chromatography (alumina grade IV; light petroleum) gave the isomeric mixture of hydrocarbons (10 mg). Further purification by t.l.c. (silica gel HF 254; light petroleum) yielded a mixture of the two isomers,  $\lambda_{\max}$  273, 283, and 296 nm;  $\nu_{\max}$  1635, 958, and 768  $\text{cm}^{-1}$ ;  $\delta$  0.90 (12H, dt,  $J$  7 and 1.5 Hz), 1.20—1.45 (8H, m), [1.72 (s), 1.76 (s), and 1.80 (s) (12H)], 1.90—2.45 (8H, m), and 5.63—6.30 (8H, m) [Found:  $M^+$ , 192.187 (100%)].

*trans*,*cis*,*cis*- and *trans*,*trans*,*cis*-4,9-Dimethyldodeca-4,6,8-triene (11a) and (10a).—(a) A mixture of *cis*-3-methylhex-2-enal (100 mg, 0.9 mmol), *trans*-3-methylhex-2-enyltriphenylphosphonium bromide (300 mg, 1.14 mmol), and 1,2-epoxybutane (1 ml) was heated in a sealed tube at 100 °C for 12 h. The product was worked up as usual and distilled (short-path) to give the mixture of isomers of the triene hydrocarbon as an oily liquid (105 mg, 75%), b.p. 80° at 0.2 mmHg. The two isomers were separated by t.l.c. [30% silver nitrate-impregnated silica gel H plates; light petroleum; Rhodamine G.6 (0.5% solution in ethanol) as indicator] to give: (i) the *trans*,*cis*,*cis*-hydrocarbon as an oil,  $\lambda_{\max}$  272.5, 282.5, and 295 nm (relative intensities 79 : 100 : 73);  $\nu_{\max}$  1640 and 758  $\text{cm}^{-1}$ ;  $\delta$  0.95 (6H, t,  $J$  7 Hz), 1.15—1.67 (4H, m), 1.90—2.37 (4H, m), 1.72 (3H, s), 1.80 (3H, s), and 5.80—6.28 (4H, m) (Found:  $M^+$ , 192.187.  $\text{C}_{14}\text{H}_{24}$  requires  $M$ , 192.188);  $m/e$  192 (100%), 163 (15,  $M - 29$ ,  $m^*$  138.4,  $163^2/192 = 138.5$ ), and 149 (6,  $M - 43$ ,  $m^*$  115.6,  $149^2/192 = 115.6$ ); and (ii) the *trans*,*trans*,*cis*-hydrocarbon as an oil,  $\lambda_{\max}$  272.5, 283, and 295.5 nm (relative intensities 74 : 100 : 78);  $\nu_{\max}$  1640 and 956  $\text{cm}^{-1}$ ;  $\delta$  0.90 (3H, dt,  $J$  7 and 1.5 Hz), 1.10—1.65 (4H, m), 1.72 (3H, s), 1.76 (3H, s), 2.02 (4H, t,  $J$  8 Hz), and [5.75 (m), 6.14 (m) (4H)] (Found:  $M^+$ , 192.187);  $m/e$  192 (100%), 163 (25,  $M - 29$ ,  $m^*$  138.4,  $163^2/192 = 138.5$ ), and 149 (10,  $M - 43$ ,  $m^*$  115.6,  $149^2/192 = 115.6$ ). The ratio of (10a) to (11a) was 2 : 3.

(b) The condensation (using potassium hydroxide and propan-2-ol) of the *trans*-aldehyde and the '*cis*-salt,' after the usual work-up, gave a mixture of isomers of the triene hydrocarbon (10%);  $\lambda_{\max}$  272.5, 282.5, and 295.5 nm;  $\nu_{\max}$  1640, 965, and 760  $\text{cm}^{-1}$ ;  $\delta$  0.89 (6H, dt,  $J$  7 and 2 Hz), 1.3—4.1 (8H, m), [1.72 (s), 1.76 (s), 1.80 (s) (6H)], and 5.70—6.45 (4H, m) (Found:  $M^+$ , 192.187).

(c) A mixture of the *trans*-aldehyde (20 mg), the *cis*-Wittig salt (100 mg), and 1,2-epoxybutane was heated in a sealed tube at 100 °C for 12 h. The usual work-up gave a

<sup>25</sup> M. Fetizon, M. Golfier, M. Maurice, and M. Janot, *Compt. rend.*, 1968, **267C**, 901.

<sup>26</sup> J. M. J. Tronchet, J. Tronchet, and A. Birkhauser, *Helv. Chim. Acta*, 1970, **53**, 1489.

mixture of isomeric hydrocarbons (22.3 mg, 65%);  $\lambda_{\max}$  272.5, 282.5, and 295.5 nm;  $\nu_{\max}$  1640, 956, and 758  $\text{cm}^{-1}$ ;  $\delta$  0.89 (6H, dt,  $J$  7 and 2 Hz), 1.1—4.3 (8H, m), [1.71 (s), 1.75 (s), 1.80 (s) (6H)], and 5.70—6.3 (4H, m) (Found:  $M^+$ , 192.187).

*cis- and trans-Methyl 3,7-Dimethyloct-2-enoate* (4b) and (3b).—Solutions of sodium methoxide [from sodium (1.2 g)] in methanol (100 ml), and 6-methylheptan-2-one<sup>27</sup> (2.85 g, 0.015 mol) in dry ether (100 ml) were added at the same rate, but separately, over 15 min to a solution of methoxycarbonylmethyl diethyl phosphonate<sup>24</sup> (5.75 g, 0.025 mol) in ether (250 ml). The solution was stirred for 15 min and diluted with water (300 ml). The ether layer was separated, and the aqueous layer extracted with ether (3  $\times$  100 ml). The combined ethereal extracts were washed with water and dried. Evaporation of the solvent and distillation of the residue gave a liquid, a mixture of the *cis-* and *trans-*esters (3.5 g, 83%), b.p. 58—59° at 0.2 mmHg. Preparative g.l.c. (23% diethylene glycol succinate column; 125°) yielded (i) the *cis-ester*,  $\lambda_{\max}$  217 nm ( $\epsilon$  11,400);  $\nu_{\max}$  1720 and 1650  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.87 (6H, d,  $J$  6 Hz), 1.88 (3H, d,  $J$  1.5 Hz), 1—2.8 (7H, m), 3.67 (3H, s), and 5.66 (1H, m) (Found:  $M^+$ , 184.146.  $\text{C}_{11}\text{H}_{20}\text{O}_2$  requires 184.146);  $m/e$  184 (70%), 152 (25,  $M - 32$ ,  $m^*$  125.5,  $152^2/184 = 125.5$ ), and 114 (100), and (ii) the *trans-ester*,  $\lambda_{\max}$  216 nm ( $\epsilon$  12,500);  $\nu_{\max}$  1717 and 1642  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.87 (6H, d,  $J$  6 Hz), 1—2.5 (7H, m), 2.15 (3H, d,  $J$  1.3 Hz), 3.67 (2H, s), and 5.66 (1H, m) (Found:  $M^+$ , 184.146);  $m/e$  184 (21%), 152 (60,  $M - 32$ ,  $m^*$  125.5,  $152^2/184 = 125.5$ ), and 114 (100). The ratio of (4b) to (3b) was 2 : 3.

*cis- and trans-3,7-Dimethyloct-2-en-1-ol*.—(a) Lithium aluminium hydride (100 mg) was added in small portions to the preceding *trans-ester* (600 mg) in dry ether (10 ml). The mixture was stirred for 1 h and ethyl acetate (1 ml) was added. A saturated solution of ammonium chloride (1 ml) was then added, and the ether layer separated. The aqueous layer was extracted with ether (3  $\times$  100 ml) and the combined extracts were dried and evaporated. Distillation of the residue (437 mg, 86%) gave the *trans-alcohol*, b.p. 80—86° at 0.045—0.5 mmHg;  $\lambda_{\max}$  204 nm;  $\nu_{\max}$  3390, 1665, 1390, 1370, 1240, and 1015  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.89 (6H, d,  $J$  8 Hz), 1.27 (5H, m), 1.58 (1H, s, exchanges with  $\text{D}_2\text{O}$ ), 1.71 (3H, s), 2.03 (2H, t,  $J$  7 Hz), 4.15 (2H, d,  $J$  7 Hz), and 5.41br (1H, t,  $J$  7 Hz) (Found:  $M^+$ , 156.151.  $\text{C}_{10}\text{H}_{20}\text{O}$  requires  $M$ , 156.150);  $m/e$  156 (5%), 138 (7,  $M - 18$ ,  $m^*$  122,  $138^2/156 = 122.08$ ), 123 (100), and 71 (100).

(b) Reduction of the *cis-ester* by a similar method yielded the *cis-alcohol* (84%); b.p. 70—76° at 0.1 mmHg;  $\lambda_{\max}$  205 nm;  $\nu_{\max}$  3390, 1670, 1380, 1375, 1245, 1175, and 1015  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.88 (6H, d,  $J$  6 Hz), 1.06 (1H, m, exchanges with  $\text{D}_2\text{O}$ ), 1.26 (5H, m), 1.75 (3H, d,  $J$  1 Hz), 2.03 (2H, m), 4.01 (2H, d,  $J$  7 Hz), and 5.41 (1H, t,  $J$  7 Hz) (Found:  $M^+$ , 156.151);  $m/e$  156 (3%), 138 (6,  $M - 18$ ,  $m^*$  122,  $138^2/156 = 122.08$ ), and 71 (100).

*trans-3,7-Dimethyloct-2-enyltriphenylphosphonium Bromide* (5b).—A mixture of *trans-3,7-dimethyloct-2-en-1-ol* (400 mg) in dry methanol (20 ml) and triphenylphosphonium bromide (1.1 g) was stirred at 20 °C for 4 days. Evaporation of the solvent, and crystallisation of the residue from chloroform and ethyl acetate gave the salt (500 mg, 52%), m.p. 186—187°;  $\delta$  ( $\text{CDCl}_3$ ) 0.80 (6H, d,  $J$  6 Hz), 1—2.5 (7H, m), 1.37 (3H, d,  $J$  4 Hz), 4.55 (2H, dd,  $J$  8 and 15 Hz), 5.05 (1H, m), and 7.73 (15H, m).

*trans-3,7-Dimethyloct-2-en-1-ol* (6b).—(a) Traces of

moisture were removed from a suspension of Fetizon's reagent<sup>25,26</sup> [silver carbonate—Celite (3.5 g)] in benzene (50 ml) by azeotropic distillation. The mixture was cooled and then the *trans-alcohol* (310 mg) in benzene (10 ml) was added. The mixture was boiled for 1 h and cooled. Filtration, and evaporation of the filtrate, followed by distillation (short-path) gave the *trans-aldehyde* as a liquid (278 mg, 90%); b.p. 82° at 0.15 mmHg;  $\lambda_{\max}$  231 nm;  $\nu_{\max}$  2755, 1680, and 1610  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.88 (6H, d,  $J$  6 Hz), 1.03—2.5 (7H, m), 2.5 (3H, d,  $J$  1.5 Hz), 5.85 (1H, dq,  $J$  7.5 and 1 Hz), and 9.98 (1H, d,  $J$  8 Hz). It gave a 2,4-dinitrophenylhydrazone, m.p. 125° (from ethanol),  $\lambda_{\max}$  (EtOH) 385, 291, and 255 nm ( $\epsilon$  19,800, 7900, and 11,600) (Found:  $M^+$ , 334.164.  $\text{C}_{16}\text{H}_{22}\text{N}_4\text{O}_4$  requires  $M$ , 334.164);  $m/e$  334 (40%), 263 (5,  $M - 71$ ,  $m^*$  207,  $263^2/334 = 207.01$ ), 249 (25,  $M - 85$ ,  $m^*$  185.5,  $249^2/334 = 185.6$ ), and 43 (100).

(b) Manganese dioxide (2.5 g) was added in small portions to *trans-3,7-dimethyloct-2-en-1-ol* (200 mg, 1.3 mmol) in light petroleum (10 ml). The mixture was stirred at 25 °C for 3 h, then filtered and evaporated. Distillation of the residue gave the *trans-aldehyde* as an oily liquid (95 mg, 42%), b.p. 58—62° at 0.1 mmHg.

(c) 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (250 mg, 1.5 mmol) was added in portions to a stirred solution of the *trans-alcohol* (200 mg, 1.3 mmol) in light petroleum (5 ml). The mixture was diluted with dichloromethane (5 ml) and chromatographed (silica gel column; 1 : 9 acetone—light petroleum) to give a mixture of stereoisomers of the aldehyde (150 mg, 95%).

*cis-3,7-Dimethyloct-2-en-1-ol* (7b).—A similar oxidation with Fetizon's reagent<sup>25,26</sup> of the *cis-alcohol* yielded the *cis-aldehyde* (85%); b.p. (air bath) 80—85° at 0.1 mmHg;  $\lambda_{\max}$  230 nm;  $\nu_{\max}$  2750, 1717, 1675, and 1630  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 0.88 (6H, d,  $J$  6 Hz), 1.66—2.75 (7H, m), 1.98 (3H, d,  $J$  1.5 Hz), 5.88br (1H, d,  $J$  8 Hz), and 9.98 (1H, d,  $J$  8 Hz). It gave a 2,4-dinitrophenylhydrazone, m.p. 105° (from ethanol);  $\lambda_{\max}$  (EtOH) 384, 290, and 256.5 nm ( $\epsilon$  21,100, 8900, and 12,800) (Found:  $M^+$ , 334.164.  $\text{C}_{16}\text{H}_{22}\text{N}_4\text{O}_4$  requires  $M$ , 334.164);  $m/e$  334 (60%), 263 (7,  $M - 71$ ,  $m^*$  207,  $263^2/334 = 207.01$ ), 43 (100), and 41 (100).

*trans,trans,trans- and trans,cis,trans-2,6,11,15-Tetramethylhexadeca-6,8,10-triene* (8b) and (9b).—*trans-3,7-Dimethyloct-2-en-1-ol* (200 mg, 1.3 mmol), *trans-3,7-dimethyloct-2-enyltriphenylphosphonium bromide* (500 mg, 1.4 mmol), and 1,2-epoxybutane (0.5 ml) were heated in a sealed tube at 100 °C for 12 h. The solvent was evaporated and the residue was dissolved in the minimum volume of chloroform and chromatographed (silica gel column; light petroleum). Further purification by preparative t.l.c. (silica gel HF<sub>254</sub>; light petroleum) gave as an oily liquid (349.5 mg, 80%) the mixture of *triene hydrocarbons*;  $\lambda_{\max}$  273.5, 284, and 296 nm;  $\nu_{\max}$  1640, 1470, 958, and 765  $\text{cm}^{-1}$ ;  $\delta$  0.88 (12H, d,  $J$  6 Hz), 1.03—2.15 (14H, m), 1.72 (6H, s), and 5.60—6.26 (4H, m);  $\delta$  ( $\text{CCl}_4$ ; 220 MHz) 0.89 (12H, d,  $J$  6 Hz), 1.04—2.18 (14H, m), 1.72 (6H, s), and [5.72 (m), 5.97 (m), 6.18 (m) (4H)] (Found:  $M^+$ , 276.282.  $\text{C}_{20}\text{H}_{36}$  requires  $M$ , 276.281);  $m/e$  276 (100%) and 205 (9,  $M - 71$ ,  $m^*$  152.2,  $205^2/276 = 152.3$ ).

*trans,cis,cis- and trans,trans,cis-2,6,11,15-Tetramethylhexadeca-6,8,10-triene* (11b) and (10b).—In a similar reaction the *cis-aldehyde* and the *trans-Wittig salt* gave an isomer mixture of the *triene hydrocarbons* (76%);  $\lambda_{\max}$  273,

<sup>27</sup> O. Wallach, *Annalen*, 1915, **408**, 185.

283.5, and 296 nm;  $\nu_{\max}$  1640, 1470, 965, and 772  $\text{cm}^{-1}$ ;  $\delta$  0.88 (12H, d,  $J$  6 Hz), 1.05—2.20 (14H, m), [1.72 (s), 1.75 (s), 1.80 (s) (6H)], and 5.64—6.22 (4H, m) [Found:  $M^+$ , 276.281 (100%).  $\text{C}_{20}\text{H}_{36}$  requires  $M$ , 276.281].

*trans,trans,trans- and trans,cis,trans-2,6,11,15-Tetramethylhexadeca-2,6,8,10,14-pentaene* (8c) and (9c).—(a) Butyl-lithium [0.2 ml, 2 mmol (from a 4.5N-solution in ether)] was added slowly to a stirred suspension of geranyltriphenylphosphonium bromide<sup>27</sup> (450 mg, 0.9 mmol) in dry ether (5 ml) and the mixture was stirred at 20 °C for 30 min. Then *trans*-citral<sup>18</sup> (100 mg, 0.7 mmol) in dry ether (5 ml) was added and the mixture boiled under reflux for 2 h. The mixture was cooled and evaporated, and the residue was dissolved in methanol (20 ml). The solution was extracted with light petroleum (3 × 20 ml) and the combined extracts were dried and evaporated. The residue was chromatographed (alumina grade IV column; light petroleum). Preparative t.l.c. (silica gel HF 254; light petroleum) yielded a mixture of the isomeric hydrocarbons as an oily liquid (98 mg, 56%),  $\lambda_{\max}$  275.5, 285.5, and 297.5 nm ( $\epsilon$  33,100, 42,200, and 31,800);  $\nu_{\max}$  1640, 960, and 755  $\text{cm}^{-1}$ ;  $\delta$  1.59 (6H, s), 1.67 (6H, s), 1.75 (6H, s), 2.09 (8H, t,  $J$  3 Hz), 5.08 (2H, m), and 5.7—6.5 (4H, m);  $\delta$  ( $\text{CCl}_4$ ; 220 MHz) 1.58 (6H, s), 1.68 (6H, s), 1.75 (6H, s), 2.10 (8H, m), 5.06br (2H, s), and [5.95 (m), 6.08 (m), 6.30 (m) (4H)] (Found:  $M^+$ , 272.250.  $\text{C}_{20}\text{H}_{32}$  requires  $M$ , 272.250);  $m/e$  272 (25%), 203 (25,  $M - 69$ ,  $m^*$  151.6, 203<sup>2</sup>/272 = 151.57), and 69 (100).

(b) A mixture of *trans*-citral<sup>18</sup> (340 mg), geranyltriphenylphosphonium bromide<sup>28</sup> (1.5 g), and 1,2-epoxybutane (1 ml) was heated in a sealed tube at 100 °C for 12 h. The product was cooled, dissolved in methanol (20 ml), and extracted with light petroleum (3 × 20 ml). The extracts were dried and evaporated and the residue was purified in the usual manner to yield the isomeric hydrocarbons (475 mg, 68%).

*trans,trans,cis- and trans,cis,cis-2,6,11,15-Tetramethylhexadeca-2,6,8,10,14-pentaene* (10c) and (11c).—A condensation of *cis*-citral<sup>18</sup> and geranyltriphenylphosphonium bromide<sup>28</sup> in 1,2-epoxybutane by the above method yielded as an oil the mixture of hydrocarbons (65%),  $\lambda_{\max}$  275.5, 285.5, and 297.5 nm ( $\epsilon$  29,800, 37,700, and 28,300);  $\nu_{\max}$  1640, 965, and 772  $\text{cm}^{-1}$ ;  $\delta$  1.59 (6H, s), 1.64 (6H, s), [1.74 (s), 1.77 (s), 1.81 (s) (6H)], 1.88 (8H, t,  $J$  8 Hz), 5.02br (2H, s), and 5.66—6.26 (4H, m);  $\delta$  ( $\text{CCl}_4$ ; 220 MHz) 1.55 (6H, s), 1.60 (6H, s), [1.70 (s), 1.75 (s), 1.78 (s) (6H)], 5.02 (2H, m), and [5.77 (m), 5.93 (m), 6.17 (m) (4H)] (Found:  $M^+$ , 272.250.  $\text{C}_{20}\text{H}_{32}$  requires  $M^+$ , 272.250);  $m/e$  272 (30%), 203 (23,  $M - 69$ ), and 69 (100).

*Isolation of Phytoene from Carrot Oil*.<sup>5</sup>—The carrot oil (20 g) in hexane (20 ml) was added to a solution of potassium hydroxide (16 g) in water (16 ml) and methanol (60 ml). The mixture was boiled under reflux for 2 h, then cooled, and aqueous 50% potassium hydroxide (16 ml) was added. The mixture thus obtained was extracted with light petroleum until the extracts were almost colourless (1.5 l). The combined light petroleum extracts were washed with water (5 × 200 ml), dried, and evaporated to about 100 ml and then extracted with aqueous 90% methanol. The extracts were rejected and the light petroleum layer was further dried and evaporated. Column chromatography of the residue (alumina grade IV; 0—5% ether in light petroleum) gave two main bands, a less polar pale yellow

band and a more polar orange band. Further purification of the first band by column chromatography (alumina grade II; light petroleum) yielded central *cis*-phytoene (160 mg);  $\lambda_{\max}$  276, 286, and 298 nm ( $\epsilon$  35,100, 43,000, and 30,700);  $\nu_{\max}$  1640 and 768  $\text{cm}^{-1}$ ;  $\delta$  1.58 (18H, s), 1.64 (6H, s), 1.74 (6H, s), 1.82—2.40 (24H, m), 5.01 (6H, m), and 5.8—6.25 (4H, m);  $\delta$  ( $\text{CCl}_4$ ; 220 MHz) 1.58 (12H, s), 1.60 (6H, s), 1.65 (6H, s), 1.74 (6H, s), 2.00 (24H, m), 5.03 (6H, m), and [5.95 (m), 6.18 (m) (4H)] (Found:  $M^+$ , 544.999. Calc. for  $\text{C}_{40}\text{H}_{64}$ :  $M$ , 544.500);  $m/e$  544 (30%), 476 (1,  $M - 68$ ), 339 (7,  $M - 205$ ,  $m^*$  211.2, 339<sup>2</sup>/544 = 211.25), and 69 (100).

*8-cis- and -trans-2,6,10,14,19,23-Hexamethyltetracos-2,6,8,10,14,18,22-heptaene* ( $\text{C}_{30}$  Model Phytoene) (12).—A mixture of *trans*-citral<sup>18</sup> (50 mg), geranylgeranyltriphenylphosphonium bromide<sup>5</sup> (175 mg), and 1,2-epoxybutane (0.2 ml) was heated in a sealed tube at 100 °C for 13 h. Evaporation of the solvent and column chromatography of the residue on alumina (grade IV) yielded a mixture of isomers of the hydrocarbon as an almost colourless oil (70 mg, 56%);  $\lambda_{\max}$  275.5, 286, and 298 nm ( $\epsilon$  31,200, 39,100, and 28,600);  $\nu_{\max}$  1640, 960, 768, 748, and 724  $\text{cm}^{-1}$ ;  $\delta$  1.58 (12H, s), 1.64 (6H, s), 1.74 (6H, s), 2.05 (16H, m), 5.04br (4H, s), and 5.5—6.5 (4H, m) (Found:  $M^+$ , 408.375. Calc. for  $\text{C}_{30}\text{H}_{48}$ :  $M$ , 408.376),  $m/e$  408 (2%), 340 (4,  $M - 68$ ), 339 (4,  $M - 69$ ), and 43 (100) [lit.<sup>5</sup> mixture of isomers,  $\lambda_{\max}$  (EtOH) 285 nm ( $\epsilon$  38,800), inflections at 297 and 273 nm;  $\nu_{\max}$  953 and 764  $\text{cm}^{-1}$ ].

*Methyl 2-cis- and -trans-3,7,11,15-Tetramethylhexadeca-2,6,10,14-tetraenoate* (4d) and (3d).—To a stirred solution of methoxycarbonyl methyl diethyl phosphonate<sup>24</sup> (650 mg, 0.2 mmol) in dry redistilled dimethylformamide (500 ml) were added farnesyl acetone (500 mg, 0.2 mmol) in dimethylformamide (20 ml) and methanolic sodium methoxide [from sodium (500 mg) in methanol (20 ml)]. The mixture was stirred at 20 °C for 2 h, boiled under reflux for 10 h, and cooled. The product was poured into water and 2% acetic acid (50 ml) was added. The mixture was extracted with ether (3 × 50 ml) and the extracts were washed with water, dried, and evaporated. Distillation (150° at 0.5 mmHg) of the residue gave as a liquid a mixture of the *cis*- and *trans*-esters (549 mg, 91%). Preparative t.l.c. (silica gel HF 254; 1:1 ether-light petroleum) gave: (i) the *cis*-ester, b.p. (air bath) 123° at 0.015 mmHg;  $\lambda_{\max}$  (EtOH) 219 nm;  $\nu_{\max}$  1745, 1725, 1600, 1440, and 1160  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 1.61 (9H, s), 1.68 (3H, s), 0.97—3.1 (12H, m), 1.88 (3H, d,  $J$  1.5 Hz), 3.67 (3H, s), 5.1br (3H, s), and 5.65br (1H, s) (Found:  $M^+$ , 318.255.  $\text{C}_{21}\text{H}_{34}\text{O}_2$  requires  $M$ , 318.255);  $m/e$  318 (5%) and 69 (100); and (ii) the *trans*-ester as an oil, b.p. (air bath) 125° at 0.02 mmHg;  $\lambda_{\max}$  (EtOH) 219 nm;  $\nu_{\max}$  1745, 1725, 1600, 1440, 1220, and 1145  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 1.62 (9H, s), 1.68 (3H, s), 0.97—3.1 (12H, m), 2.17 (3H, d,  $J$  1.5 Hz), 3.67 (3H, s), 5.1br (3H, s), and 5.67br (1H, s) (Found:  $M^+$ , 318.255);  $m/e$  318 (6%) and 69 (100). The ratio of (4d) to (3d) was 2:3.

*2-cis- and trans-3,7,11,15-Tetramethylhexadeca-2,6,10,14-tetraenol* (*Geranylgeraniol*).—(a) Lithium aluminium hydride (200 mg) was added slowly to methyl *trans*-3,7,11,15-tetramethylhexadeca-2,6,10,14-tetraenoate (234 mg) in dry ether (25 ml) over 5 min with stirring and the mixture was then stirred for a further 4 h. Moist ether (50 ml) was added, followed by ammonium chloride solution (5 ml). The ether layer was separated and the aqueous layer extracted with ether (3 × 50 ml). The combined ethereal extracts were washed with water, dried, and evaporated.

<sup>28</sup> O. Isler, H. Gutmann, H. Lindlar, M. Montavon, R. Rügge, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, 1956, **39**, 463.

Distillation of the residue gave all-*trans*-geranylgeraniol<sup>29</sup> (203 mg, 95%); b.p. (air bath) 126° at 0.1 mmHg;  $\nu_{\max}$  3320, 1635, 1450, 1380, and 1005 cm<sup>-1</sup>;  $\delta$  (CDCl<sub>3</sub>) 1.60 (9H, s), 1.67 (6H, s), 1.90—2.27 (12H, m), 2.35 (1H, s, exchanges with D<sub>2</sub>O), 4.10 (2H, d, *J* 7 Hz), and 5.1br (4H, s) (Found:  $M^+$ , 290.259. C<sub>20</sub>H<sub>34</sub>O requires *M*, 290.260); *m/e* 290 (1.5%) and 69 (100).

(b) A similar reduction of the *cis*-ester gave the *cis*-alcohol (95%), b.p. 120° at 0.125 mmHg;  $\nu_{\max}$  3300, 1640, 1440, 1380, and 1000 cm<sup>-1</sup>;  $\delta$  (CDCl<sub>3</sub>) 1.60 (9H, s), 1.67 (6H, s), 2.05 (12H, s), 2.60br (1H, s, exchanges with D<sub>2</sub>O), 4.10 (2H, d, *J* 7 Hz), and 5.10br (4H, s) (Found:  $M^+$ , 290.260).

2-*cis*- and -*trans*-3,7,11,15-Tetramethylhexadeca-2,6,10,14-tetraenal (Geranylcitral) (7d) and (6d).—(a) A suspension of Fetizon's reagent<sup>25,26</sup> (silver carbonate—Celite) (3 g) in benzene (25 ml) was boiled for 4 h under a Dean–Stark head. The mixture was cooled, *trans*-geranylgeraniol (250 mg, 0.87 mmol) in benzene (10 ml) was added, and the resulting mixture was heated again for 1 h. The product was cooled, filtered, and evaporated. Column chromatography [silica gel deactivated with water (10% v/w); gradient elution with light petroleum and benzene] gave as a liquid the all-*trans*-aldehyde (150 mg, 59%); b.p. (air bath) 135° at 0.025 mmHg;  $\lambda_{\max}$  (EtOH) 241.5 nm;  $\lambda_{\max}$  (hexane) 232 nm;  $\nu_{\max}$  1670 cm<sup>-1</sup>;  $\delta$  (CDCl<sub>3</sub>) 1.60 (9H, s), 1.67 (3H, s), 2.15 (3H, d, *J* 1 Hz), 2.1—3.33 (12H, m), 5.08br (3H, s), 5.88 (1H, d, *J* 8 Hz), and 9.90 (1H, d, *J* 8 Hz) (Found:  $M^+$ , 288.245. C<sub>20</sub>H<sub>32</sub>O requires *M*, 288.245); *m/e* 288 (10%), 83 (46, *M* - 205), and 69 (100).

(b) An analogous oxidation of the *cis*-alcohol and work-up gave the *cis*-aldehyde (69%),  $\lambda_{\max}$  (EtOH) 238.5 nm,  $\lambda_{\max}$  (hexane) 232 nm;  $\nu_{\max}$  1675 cm<sup>-1</sup>;  $\delta$  (CDCl<sub>3</sub>) 1.60 (9H, s), 1.67 (3H, s), 1.98 (3H, d, *J* 1 Hz), 2.0—2.8 (12H, m), 5.08br (3H, s), 5.87 (1H, d, *J* 8 Hz), and 9.88 (1H, d, *J* 8 Hz) (Found:  $M^+$ , 288.245).

15-*cis*- and all-*trans*-7,8,11,12,7',8',11',12'-Octahydrolycopene (15-*cis*- and all-*trans*-Phytoene), (9d) and (8d).—A mixture of *trans*-geranylcitral (250 mg), *trans*-geranylgeranyltriphenylphosphonium bromide<sup>5</sup> (500 mg), and 1,2-epoxybutane (1 ml) was heated in a sealed tube for 12 h. The product was cooled and evaporated. Column chromatography (alumina; grade IV; light petroleum) yielded the phytoene isomers as an almost colourless oil (275 mg, 61%);  $\lambda_{\max}$  275.5, 286, and 297.5 nm ( $\epsilon$  37,800, 46,800 and 32,600).

Column chromatography (grade I alumina, 0.5—5% ether in light petroleum) gave: (i) 15-*cis*-phytoene,  $\lambda_{\max}$  276, 286, and 298 nm ( $\epsilon$  36,300, 43,100, and 32,100);  $\nu_{\max}$  1640, 1605, and 758 cm<sup>-1</sup>;  $\delta$  1.57 (18H, s), 1.65 (6H, s), 1.73 (6H, s), 2.00 (24H, m), 5.02 (6H, m), and 5.8—6.35 (4H, m);  $\delta$  (CCl<sub>4</sub>; 220 MHz) 1.58 (12H, s), 1.60 (6H, s), 1.65 (6H, s), 1.74 (*ca.* 6H, s), 2.00 (24H, m), 5.01 (6H, m), and [5.95 (m), 6.18 (m) (4H)] [a weak signal at 1.81 indicated contamination (<10%) with the *trans,cis,cis*-isomer] (Found:  $M^+$ , 544.501. Calc. for C<sub>40</sub>H<sub>64</sub>: *M*, 544.500);

*m/e* 544 (9%), 476 (2.2, *M* - 68), 339 (4, *M* - 205, *m*\* 211.2, 339<sup>2</sup>/544 = 211.25), and 69 (100); and (ii) all-*trans*-phytoene:  $\lambda_{\max}$  275, 286, and 298 nm ( $\epsilon$  30,900, 45,400, and 32,700);  $\nu_{\max}$  1640, 1605, and 950 cm<sup>-1</sup>;  $\delta$  1.58 (18H, s), 1.67 (6H, s), 1.75 (6H, s), 2.00 (24H, m), 5.01 (6H, m), and 5.6—6.35 (4H, m);  $\delta$  (CCl<sub>4</sub>; 220 MHz) 1.58 (12H, s), 1.60 (6H, s), 1.65 (6H, s), 1.74 (6H, s), 2.00 (24H, m), 5.01 (6H, m), and [5.81 (m), 6.18 (m) (4H)] [a weak signal at 1.77 indicated contamination (<10%) with the *trans,trans,cis*-isomer] (Found:  $M^+$ , 544.501); *m/e* 544 (8%), 476 (3, *M* - 68), 339 (4, *M* - 205, *m*\* 211.2, 339<sup>2</sup>/544 = 211.25), 205 (5), and 69 (100). The *cis*-isomer accounted for 20% of the mixture.

*trans,trans,cis*- and *trans,cis,cis*-Phytoene (10d) and (11d).—The analogous reaction between *cis*-geranylcitral and the *trans*-geranylgeranyl Wittig salt<sup>5</sup> gave a mixture of the required phytoene isomers (60%),  $\lambda_{\max}$  275.5, 285.5, and 298 nm;  $\nu_{\max}$  1640, 960, and 766 cm<sup>-1</sup>;  $\delta$  1.58 (18H, s), 1.65 (6H, s), [1.74 (s), 1.77 (s), 1.82 (s) (6H)], 2.04 (24H, m), 5.04 (6H, m), and 5.6—6.4 (4H, m);  $\delta$  (CCl<sub>4</sub>; 220 MHz) 1.56 (12H, s), 1.60 (6H, s), 1.65 (6H, s), [1.74 (s), 1.77 (s), 1.81 (s) (6H)], 2.04 (24H, m), 5.04 (6H, m), and [5.81 (m), 5.95 (m), 6.81 (m) (4H)] (Found:  $M^+$ , 544.499); *m/e* 544 (18%), 476 (5, *M* - 68), 408 (2, *M* - 136), 339 (9, *M* - 205, *m*\* 211, 339<sup>2</sup>/544 = 211.2), 81 (100), and 69 (100).

Iodine-catalysed Photoisomerisation of all-*trans*-Phytoene.—A solution of all-*trans*-phytoene (8d) (5 mg) in light petroleum (5 ml) containing a trace of iodine was irradiated (100 W tungsten lamp at a distance of 10 cm) for 30 min to give a mixture of isomers,  $\lambda_{\max}$  275, 285.5, and 298 nm (1.06 : 1.41 : 1);  $\nu_{\max}$  1640, 960, and 767 cm<sup>-1</sup>;  $\delta$  1.57 (18H, s), 1.65 (6H, s), 1.73 (6H, s), 2.00 (24H, m), 5.02 (6H, m), and 5.7—6.4 (4H, m);  $\delta$  (CCl<sub>4</sub>; 220 MHz) 1.57 (12H, s), 1.60 (6H, s), 1.65 (6H, s), [1.73 (s), 1.77 (s), 1.81 (s) (6H)], 2.00 (24H, m), 5.04 (6H, m), and [5.80 (m), 5.95 (m), 6.18 (m) (4H)] (Found:  $M^+$  544.500).

Iodine-catalysed Stereoisomerisation of (Natural) 15-*cis*-Phytoene.—A solution of natural phytoene (20 mg) in light petroleum (5 ml) containing a trace of iodine was irradiated (30 min; 100 W tungsten lamp at a distance of 30 cm) to give a mixture of isomers,  $\lambda_{\max}$  275.5, 286, and 298 nm (1.12 : 1.39 : 1);  $\nu_{\max}$  1670, 1635, 980, 960, and 770 cm<sup>-1</sup>;  $\delta$  1.55 (18H, s), 1.64 (6H, s), [1.74 (s), 1.80 (s) (6H)], 2.03 (24H, m), 5.02 (6H, m), and 5.6—6.4 (4H, m);  $\delta$  (CCl<sub>4</sub>; 220 MHz) 1.58 (12H, s), 1.60 (6H, s), 1.64 (6H, s), [1.74 (s), 1.77 (s), 1.81 (s) (4H)], 2.06 (24H, m), 5.02 (6H, m), and [5.81 (m), 5.95 (m), 6.18 (m) (4H)] (Found:  $M^+$ , 544.500); *m/e* 544 (5%), 339 (2, *M* - 205), and 69 (100).

We thank Hoffman-La Roche Ltd. for gifts of chemicals, and Roche Products Ltd. for financial support. We are indebted to the Association of Commonwealth Universities for a research scholarship (to N. K.), and to Queen Mary College for a research studentship (to D. E. L.).

[5/026 Received, 7th January, 1975]

<sup>29</sup> E. Fedeli, M. Capella, M. Cirimele, and G. Jacini, *J. Lipid Res.*, 1966, **7**(3), 437.