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## Carotenoids and Related Compounds. Part XIV.<sup>1</sup> Stereochemistry and Synthesis of Geraniol, Nerol, Farnesol, and Phytol

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The cis- and trans-structures assigned to nerol and geraniol respectively have been confirmed.

The trans, trans-structure of the common form of farnesol, and of the farnesyl pyrophosphate involved in the biosynthesis of squalene, has been rigorously established.

Phytol has been shown to have a trans-configuration about the double bond, and an R-configuration at both asymmetric centres.

At the commencement of these studies little information was available concerning the stereochemistry of the acyclic terpenes containing primary allylic systems. Geraniol (Va) was believed to have the trans-configuration \* because it cyclises in acids to  $\alpha$ -terpineol more slowly than its geometrical isomer, nerol.<sup>2</sup> Farnesol

\* With trisubstituted double bonds, the terms cis and trans are used to designate the relative positions of the two largest substituents.

<sup>1</sup> Part XIII, A. P. Leftwick, and B. C. L. Weedon, Acta Chem. Scand., 1966, 20, 1195.
<sup>2</sup> O. Zeitschel, Ber., 1906, 39, 1780.
<sup>3</sup> P. de Mayo, "Mono- and Sesqui-terpenes," Interscience,

New York, 1959.

<sup>4</sup> F. G. Fischer and K. Löwenberg, Annalen, 1929, 475, 183. <sup>5</sup> P. Karrer and B. H. Ringier, Helv. Chim. Acta, 1939, 22, 610.

<sup>6</sup> P. Karrer and E. Bretscher, Helv. Chim. Acta, 1943, 26, 1758.

(Vb) was formulated as the trans, trans-isomer mainly by analogy with geraniol.<sup>3</sup> Neither the geometrical nor the optical configuration of phytol (Vc) was known, despite numerous "syntheses" of the alcohol and related compounds.4-15 This situation was all the more

<sup>7</sup> L. I. Smith and J. A. Sprung, J. Amer. Chem. Soc., 1943, 65, 1276. \* L. I. Smith and G. F. Roualt, J. Amer. Chem. Soc., 1943,

**65**, 745. <sup>9</sup> Brit. Pat. 633,711.

- <sup>10</sup> J. D. Cawley, Brit. Pat. 728,446.
   <sup>11</sup> R. Lukeš and A. Zobáčová, *Chem. listy*, 1957, **51**, 330.
   <sup>12</sup> J. Weichet, J. Hodravá, V. Kvita, *Chem. listy*, 1957, **51**, 568.
- <sup>13</sup> I. K. Sarycheva, G. A. Vorob'eva, N. A. Kuznetsova, and N. A. Preobrazhenskii, Zhur. obshchei Khim., 1958, 28, 647.
- 14 V. I. Gunar, B. P. Gussev, and I. N. Nazarov, Zhur. obshchei Khim., 1958, 28, 1444.
- <sup>15</sup> V. I. Gunar and S. I. Zav'yalov, Doklady, Akad. Nauk. S.S.S.R., 1960, 132, 829.

surprising in view of the availability of these terpenes, and the importance which they and their derivatives have in nature. In this Paper we report the solution of these stereochemical problems by nuclear magnetic resonance (n.m.r.) spectroscopy and synthesis; brief accounts of our main findings have been given previously.16-18

Geometrical Configurations.—All the double bonds now under consideration are trisubstituted. Stereochemical assignments in such systems can frequently be made by n.m.r. spectroscopy, provided that the geometrical isomer of the compound being studied, or a suitable mixture of the two isomers, is available for comparison.<sup>19</sup> Since spectrometers operating at frequencies greater than 40 Mc./sec. were not available when the work now reported was begun, it was decided to relate the terpene alcohols (V) to the corresponding aldehydes (VI) and esters (III). In this way it was possible to take advantage of the specially favourable differences which exist in the n.m.r. spectra of geometrical isomers of trisubstituted olefins when one carbon atom of the double bond carries a methyl group and the other a carbonyl group.19



Attempts were first made to oxidise the alcohols to the corresponding aldehydes (VI) with manganese dioxide, a selective reagent which, in the vitamin A series for example,<sup>20</sup> causes no stereomutation. Although geraniol and nerol gave mainly trans-citral (identical with "citral a") and cis-citral (identical with "citral b"), respectively, the yield and stereochemical purity of the product varied greatly with the source of the reagent (see Experimental section).

Oxidation of phytol (derived from chlorophyll) with manganese dioxide gave phytenal (VIc) which, from its n.m.r. spectrum, consisted mainly, if not entirely, of the trans-isomer. [Similar oxidation of a synthetic

<sup>16</sup> J. W. K. Burrell, L. M. Jackman, and B. C. L. Weedon, Proc. Chem. Soc., 1959, 263.

 <sup>17</sup> B. C. L. Weedon, *Adv. Org. Chem.*, 1960, **1**, 1.
 <sup>18</sup> B. C. L. Weedon, Abs. Comm. 2nd Internat. Symp. Chem. Nat. Prod., Prague, 1962, p. 91.
 <sup>19</sup> L. M. Jackman, "Applications of Nuclear Magnetic Reson-

ance Spectroscopy in Organic Chemistry," Pergamon, London, 1959

<sup>20</sup> Sir Ian Heilbron and B. C. L. Weedon, Bull. Soc. chim. France, 1958, 83.

phytol prepared by isomerisation of  $(\pm)$ -isophytol (IVc)<sup>21</sup> gave the expected mixture of cis- and trans- $(\pm)$ -phytenal.] However, oxidation of the aldehyde from natural phytol with silver oxide, and esterification of the product, gave a methyl phytenoate (IIIc) which was shown by chromatography to contain some of the cis-isomer. The latter presumably arose from a partial loss of configuration during one of the oxidation stages, since it was found subsequently (see below) that natural phytol is homogeneous.

The methyl esters (III) corresponding to the terpene alcohols (V) were readily prepared by reaction of the appropriate methyl ketones (I) with methoxyacetylene, and isomerisation of the resulting acetylenic alcohols (II) with acid.<sup>22</sup> Thus methylheptenone (Ia) was converted into a mixture of methyl geranates (IIIa) which was separated by chromatography into two isomers whose configurations were assigned from the relative positions of the C-3 methyl absorption bands in the n.m.r. spectra. Reduction of the cis- and trans-esters with lithium aluminium hydride gave nerol and geraniol. respectively. Since the carbon-carbon double bonds are not implicated in these reductions, nerol must have the cis-, and geraniol the trans-configuration, as previously proposed.

Similarly, cis-geranyl acetone (Ib)<sup>21</sup> was converted into cis-2, cis-6- and trans-2, cis-6-methyl farnesoate (IIIb), and trans-geranyl acetone into cis-2, trans-6- and trans-2, trans-6-methyl farnesoates. The configuration at both the 2,3- and 6,7-double bonds was readily determined by examination of the n.m.r. spectra. Reduction of the four esters individually with lithium aluminium hydride gave the corresponding alcohols (Vb) which, like the esters, could be resolved by gasliquid chromatography under appropriate conditions. (The synthesis, by the same general route, of a mixture of farnesols believed to consist of the cis-2, trans-6- and trans-2, trans-6-isomers has been reported by Popják and Cornforth.<sup>23</sup>) Mixed gas-liquid chromatograms (for which the authors are indebted to Dr. G. Popják) of our trans-2, trans-6-farnesol with natural farnesol (prepared by enzymatic hydrolysis of farnesyl pyrophosphate derived enzymatically from mevalonic acid 5-phosphate) showed the two to be identical. This proves conclusively that the farnesyl derivatives involved in the biosynthesis of squalene<sup>24</sup> are *trans,trans*. It also confirms that the pure stereoisomer of farnesol which is found in many essential oils is the trans-2, trans-6-form, and that the second isomer observed in petit grain and a number of other oils is the cis-2,trans-6-isomer.25

Since this work was completed, Popják et al.26 have

<sup>21</sup> O. Isler, Angew. Chem., 1959, **71**, 7; W. Kimel, N. W. Sax, S. Kaiser, G. G. Eichmann, G. O. Chase, and A. Ofner, J. Org. Chem., 1958, 23, 153.

22 Sir Ian Heilbron, E. R. H. Jones, M. Julia, and B. C. L. Weedon, J. Chem. Soc., 1949, 1823. <sup>23</sup> G. Popják and R. H. Cornforth, J. Chromatog., 1960, **4**, 214.

<sup>24</sup> Cf. J. W. Cornforth, Pure Appl. Chem., 1961, 2, 607.
 <sup>25</sup> Y.-R. Naves, Compt. rend., 1960, 251, 900.
 <sup>26</sup> G. Popják, J. W. Cornforth, R. H. Cornforth, R. Ryhage,

and DeW. S. Goodman, J. Biol. Chem., 1962, 237, 56.

described the preparation of two isotopically labelled farnesols. These were assigned trans-2, trans-6-structures in view of their mode of synthesis from a geranyl acetone regarded as trans, and from a consideration of retention data on gas-liquid chromatography. Recently Bates et al.27 have reported the isolation of the four isomeric farnesols by preparative gas-liquid chromatography of the mixtures obtained by isomerisation of cis- and trans-nerolidol (IVb). It was assumed that the main isomer formed in each rearrangement would have the trans-2-configuration, and that the values for refractive index and retention time would be highest for the trans, trans- and lowest for the cis, cis-isomer. Their n.m.r. evidence is discussed later.

Reaction of the C<sub>18</sub>-ketone (Ic), prepared by ozonolysis of (natural) phytol,28,29 with methoxyacetylene, and isomerisation of the product (IIc), gave a mixture of methyl phytenoates (IIIc) which was separated by chromatography into two isomers whose geometrical configurations were determined unambiguously by n.m.r. spectroscopy. (It is noteworthy that the *cis*-isomer was *dextro*-rotatory and the *trans*-isomer *laevo*-rotatory.) Reduction of the esters with lithium aluminium hydride gave the corresponding cis- and trans-phytols (Vc). These, like natural phytol, gave only one band on gasliquid chromatography on poly (ethylene glycol succinate). In mixed chromatograms (for which the authors thank Dr. F. W. Hobden) natural phytol separated from the cis- but not from the trans-alcohol.

An alternative route to the phytols was demonstrated by anodic crossed coupling of the 3(RS), 7(R')-trimethyldodecanoic acid (XIV) (see below) with the half ester (VII).<sup>30</sup> The latter was found to be a mixture in which the *cis*-isomer predominated,\* and thus gave rise to a similar mixture of cis- and trans-phytenoates. These were separated by chromatography and reduced to the 7(RS), 11(R')-cis- and trans-phytols.

N.m.r. Spectra.—In all the  $\alpha\beta$ -unsaturated esters examined the  $\beta$ -methyl group absorbed, as expected, at lower fields than the other olefinic methyl groups, if any, and gave rise to a doublet  $(J \sim 1-2 \text{ c./sec.})$  due to spin-spin coupling with the C- $\alpha$  proton. With each pair of isomers the cis-2-configuration was assigned to the compound in which the  $\beta$ -methyl absorption occurred at higher fields, using the correlation established by Jackman and Wiley.<sup>31</sup> The difference in absorption of the geometrical isomers (Table 1) may be ascribed to long-range deshielding of the  $\beta$ -methyl group in the trans-isomer by the ester group which is situated close

\* Originally the half ester (VII) was regarded (incorrectly) as trans by analogy with the configuration of the unmethylated half ester prepared similarly.<sup>30</sup> The difference in stereochemistry now recognised can readily be explained on conformational grounds.

27 R. B. Bates, D. M. Gale, and B. J. Grunar, J. Org. Chem., 1963, 28, 1086.

F. G. Fischer, Annalen, 1928, 464, 69.

<sup>29</sup> P. Karrer, A. Geiger, H. Reutschler, E. Zbinden, and A. Kugler, *Helv. Chim. Acta*, 1943, 26, 1741.
 <sup>30</sup> R. P. Linstead, J. C. Lunt, B. R. Shephard, and B. C. L. Weedon, *J. Chem. Soc.*, 1952, 3621.

(cis) to it. Similarly with the citrals and the phytenals the *cis*-configuration was assigned to the isomer with the  $\beta$ -methyl band at higher fields.

TABLE 1

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Ester	cis-2	trans-2	$\tau_{cis} - \tau_{trans}$
MeO_C·CMeCH·CO_Me	7.96	7.72	0.24
MeO,C·CH,·CMe:CH·CO,Me b	8.04	7.80	0.24
EtO, C·(CH,), CMe:CH·CO, Et	8.09	7.85	0.24
Methyl geranate	8.27	8.02	0.25
Methyl cis-6-farnesoate	8.10	7.78	0.32
Methyl trans-6-farnesoate	8.10	7.78	0.32
Methyl phytenoate	8.14	7.89	0.25
<sup>a</sup> For conditions, see Exper	imental	section. b	Jackman and

Wiley.31

The (unconjugated) isopropylidene group in methylheptenone, the citrals, the methyl geranates, and related compounds, gave rise to two methyl bands of equal intensity at 8.34 and 8.40.32 The C-6 methyl group in the geranyl acetones, and the C-7 methyl group in the derived farnesoates, gave a band which was superimposed on one or other of those due to the isopropylidene methyls, depending on the stereochemistry of the 5,6- and 6,7double bond, respectively. Since (all-trans) squalene exhibits methyl bands at 8.35 and 8.42 with relative intensities of  $1:3,^{33,34}$  it may be concluded that methyl substituents on *cis*- and *trans*-bonds (unconjugated) give rise to absorption near 8.34 and 8.40, respectively. The observation of methyl bands at 8.34 and 8.40 with relative intensities of 2:1 and 1:2 in the spectra of cis- and trans-geranylacetone, respectively, confirms the geometrical assignments made previously on the basis of other physical properties and the correlation of one of these ketones with trans-geraniol.35 Similarly, the relative intensities of the bands at 8.34 and 8.40 in the spectra of the farnesoates reveals the stereochemistry of the 6,7-double bond (Figure 1).

Recently, Bates and Gale 34 have drawn attention to small differences which can be observed (at 60 Mc./sec.) in the olefinic methyl bands of geraniol, nerol, and the farnesols; we have noted similar differences in the spectra of cis- and trans-phytol ( $\tau$  8.27 and 8.38, respectively). Unfortunately, the band due to a  $\beta$ -methyl group in trans-allylic alcohols cannot be resolved from that due to a methyl group attached to a cis (unconjugated) double bond, or from one of the bands associated with an (unconjugated) isopropylidene group. However, Bates et al.27 were able to use the relative intensities of absorption at 8.27, 8.34, and 8.41 to substantiate their stereochemical assignments to the four farnesols.

<sup>31</sup> L. M. Jackman and R. H. Wiley, Proc. Chem. Soc., 1958,

<sup>10</sup> L. M. Jackman and K. H. Wiley, Proc. Chem. Soc., 1958, 196; J. Chem. Soc., 1960, 2881, 2886.
 <sup>32</sup> M. S. Barber, J. B. Davis, L. M. Jackman, and B. C. L. Weedon, J. Chem. Soc., 1960, 2870.
 <sup>33</sup> Part XV, following Paper.
 <sup>34</sup> R. B. Bates and D. M. Gale, J. Amer. Chem. Soc., 1960, 82, 5749; cf. H. Rapoport and H. P. Hamlow, Biochem. Biophys. Back Comm. 1061, 6, 195.

Res. Comm., 1961, 6, 134.
 <sup>35</sup> Y.-R. Naves, Helv. Chim. Acta, 1949, 32, 1798; Perfum. Essent. Oil Record, 1949, 40, 78.

Absolute Configuration (Phytol)\*.---The optical rotation of phytol from chlorophyll is extremely small, but that of the derived  $C_{18}$ -ketone (XVI = Ic), and of the phytadienes produced on dehydration, dispel any doubts that the natural alcohol is optically active.<sup>29,37</sup> Previous studies on its stereochemistry indicated that C-7 is optically active,<sup>37</sup> and it was suggested (reasonably, but without experimental evidence) that C-11 is also active. However, the conclusion drawn<sup>29</sup> concerning the stereochemistry at C-11 was invalidated by later work.<sup>37</sup> It seemed to us that the absolute configuration

ation of an asymmetric centre (except for one at  $C-\alpha$ ) is fully preserved during anodic crossed coupling,<sup>17</sup> the product was assigned the 6(RS), 10(R')-structure.

Substitution in the above synthesis of the racemic half ester (IX;  $R = PhCH_2$ ) by the (-)-S-half ester (IX; R = Me)<sup>39</sup> gave the 6(S), 10(R')-ketone (XVI).



Assuming, as a first approximation, that the optical activities of the centres at C-6 and C-10 in the C18-ketone are independent of one another, the observed rotations of the two synthetic ketones (Table 2) indicated that R

TABLE 2 Optical rotations of the C<sub>18</sub>-ketones (l = 1, homogeneous liquid)

Configuration	$\alpha_D^{23}$
6( <i>RS</i> ),10(R')	$-0.20^{\circ}$
6(S), 10(R')	-0.98
6(R), 10(R')	+0.66
Natural	+0.57

configurations at C-6 and C-10 contribute  $ca. +0.8^{\circ}$  and  $-0.2^{\circ}$ , respectively, to the rotation: the opposite sign of these contributions is noteworthy. A 6(R), 10(R)configuration (predicted  $\alpha_{p} + 0.8^{\circ} - 0.2^{\circ} = +0.6^{\circ}$ )

<sup>37</sup> P. Karrer, H. Simon, and E. Zbinden, Helv. Chim. Acta, 1944, 27, 313.

 <sup>38</sup> A. J. Birch, Ann. Rep. Progr. Chem., 1950, 47, 191.
 <sup>39</sup> R. P. Linstead, J. C. Lunt, and B. C. L. Weedon, J. Chem. Soc., 1950, 3331, 3333.



FIGURE 1 N.m.r. spectra of the methyl farnesoates (in CCl<sub>4</sub>; 60 Mc./sec.)

of phytol could best be revealed by stereochemically controlled syntheses of the  $C_{18}$ -ketone (XVI), and some of its stereoisomers. For convenience, (+)-citronellol (X) was chosen as the starting material. Its absolute configuration has been determined,<sup>38</sup> and may be represented as R. However, for the reasons explained below, we prefer to use the symbol R' for the asymmetric centre in the sample used in our work.

Catalytic reduction of (+)-citronellol (X) gave (+)-dihydrocitronellol (XII) which was converted (via the nitrile route) into the C<sub>11</sub>-acid (XIII). Anodic crossed coupling of the latter with the racemic half ester (IX;  $R = PhCH_2$ ) led to the  $C_{15}$ -acid (XIV). This, on anodic crossed coupling with laevulic acid (XV), furnished the C<sub>18</sub>-ketone (XVI). Since the configur-

<sup>\*</sup> Absolute configurations are given as R or S using the convention of Cahn, Ingold, and Prelog.  $^{36}$ 

<sup>&</sup>lt;sup>36</sup> R. S. Cahn, C. K. Ingold, and V. Prelog, Experientia, 1956, **12**, 81.

therefore seemed probable for the "natural"  $\mathrm{C}_{18}\text{-}$ ketone (observed  $\alpha_{\rm D} = +0.57^{\circ}$ ). However, substitution of the (+)-R half ester<sup>39</sup> for its stereoisomer in the preceding synthesis gave a 6(R), 10(R')-C<sub>18</sub>-ketone, which, surprisingly, exhibited slightly higher rotation than the "natural" ketone. This discrepancy must be due to lack of optical purity, either in phytol (leading to a low rotation of the "natural" ketone), or at C-10 in the synthetic ketone (leading to a high value for the net rotation exhibited by both centres). The latter explanation seemed inherently more probable, and was confirmed by anodic crossed coupling of isohexanoic acid (VIII) with the (+)-R half ester (IX; R=Me), and reduction of the product (XI) with lithium aluminium hydride. The dihydro-citronellol (XII) thus obtained exhibited higher rotation than that derived from citronellol (X). The sample of the latter used in the present studies had been prepared by Ponndorf reduction of natural citronellal. Its optical purity was estimated as ca. 80%, (*i.e.*, ca. 10% contamination with the enantiomorph), and the configuration of the asymmetric centre was designated as R' rather than R.

There now seemed no justification in assuming a*priori* that phytol (XIX) is optically pure. The results so far described merely established that, because of its relatively high dextro-rotation, the "natural" ketone must be R, or predominantly R, at C-6. However, if it be conceded that C-6 may not be optically pure, then C-10 could conceivably be RS, partially R, or even S, to produce the algebraic sum of ca.  $+0.57^{\circ}$ for the observed net rotation of both centres. It was therefore considered necessary to confirm the provisional 6(R), 10(R)-configuration for the "natural" ketone by relating the two centres to one another.

Reaction of the " natural " C18-ketone with the methylene Wittig reagent, and catalytic reduction of the resulting olefin, gave the hydrocarbon (XVII) which exhibited no optical rotation. This inactivity can only be attributed to internal compensation since the hydrocarbon prepared similarly from the synthetic 6(RS), 10(R')ketone was laevo-rotatory. Therefore both centres in the " natural " C18-ketone must have the same configuration and, as far as can be ascertained in view of the experimental error associated with measuring low rotations, both are optically pure. It follows that phytol has the 7(R), 11(R)-trans-2-configuration, which may also be represented as D-7,D-11, trans-2 using the convention of Linstead, Lunt, and Weedon <sup>39</sup> and by the Fischer projection (XIXa). Moreover, ignoring the slight lack of optical purity at one centre in some of the intermediates, due to using citronellol as a relay in the preparation of the C<sub>18</sub>-ketone, an appropriate combin-

- 42 É. Demole, Compt. rend., 1956, 243, 1883.

 R. L. Rowland, J. Amer. Chem. Soc., 1957, 79, 5007.
 G. Eglinton, P. M. Scott, T. Belsky, A. L. Burlingame, and M. Calvin, Science, 1964, 17, 263; T. Belsky, R. B. Johns, E. D. McCarthy, A. L. Burlingame, W. Richter, and M. Calvin, Nature, 1965, 206, 446.

ation of the various preparations reported in this Paper constitutes the first total synthesis of the natural isomer.

Additional support for a 7(R)-structure in phytol has been provided by optical rotatory dispersion (o.r.d.) studies on the two degradation products (XX) and (XXI).40

Natural Compounds Related to Phytol.-In nature, phytol occurs mainly as chlorophyll, from which it is obtained by hydrolysis.<sup>41</sup> An isophytol (IVc) has been reported 42 in jasmin oil, neophytadiene (XXII) in flue cured tobacco,43 and phytane together with pristane (XVII) in some animals and ancient sediments.<sup>44</sup> The stereochemistry of these natural products has not been determined, but is probably related directly to that now established for (chlorophyll) phytol.



The phytol carbon skeleton can also be recognised in vitamin K<sub>1</sub> (XXIII), and in the tocopherols. Following our preliminary publication, Isler et al.45 demonstrated that the side chain of vitamin  $K_1$  has the same stereochemistry as that in phytol. They have also elucidated the stereochemistry of  $\alpha$ -tocopherol and shown that the two asymmetric centres in the aliphatic side chain have the same configuration as those of the corresponding centres in phytol.45



The present synthesis of phytol also completes the total synthesis of vitamin  $K_1$  (XXIII) and of "DL- $\alpha$ tocopherol" (XXIV), both of which were previously dependent on natural phytol.46-48 Recently it has been

<sup>45</sup> H. Mayer, P. Schudel, R. Rüegg, and O. Isler, *Helv. Chim. Acta*, 1963, **46**, 963; H. Mayer, U. Gloor, O. Isler, R. Rüegg, and

Atta, 1903, 40, 903, 11. Mayel, C. Globi, C. Islei, K. Ruegg, and
 O. Wiss, *ibid.*, 1964, 47, 221.
 <sup>46</sup> S. B. Binkley, L. C. Cheney, W. F. Holcomb, R. W. McKee,
 S. A. Thayer, D. W. MacCorquodale, and E. A. Doisy, J. Amer.
 Chem. Soc., 1939, 61, 2558; H. J. Almquist and A. A. Klose,
 *ibid.*, p. 2557; L. F. Fieser, *ibid.* pp. 2559, 2561, 3467; L. F. Fieser,
 M. Tishler, and N. L. Wendler, *ibid.*, 1940, 62, 2861.
 A. Lorge and K. Dochol. Hels. Chim. Acta, 1054, 27, 225.

47 O. Isler and K. Doebel, Helv. Chim. Acta, 1954, 37, 225.

48 P. Karrer, H. Fritsche, B. H. Ringier, and H. Salomon, Helv. Chim. Acta, 1938, 21, 520, 820.

P. Crabbé, C. Djerassi, E. J. Eisenbraun, and S. Liu, Proc. Chem. Soc., 1959, 264.
 R. Willstätter and F. Hocheder, Annalen, 1907, 354, 205.

confirmed that the synthesis of vitamin K<sub>1</sub> from phytol involves little stereomutation about the double bond.49 The total synthesis of chlorophyll has been reported,<sup>50</sup> but the absolute configuration of the dihydropyrrole ring has still to be determined.

## EXPERIMENTAL

Physical Measurements.-Melting points are uncorrected. Ultraviolet light absorption data were determined on ethanolic solutions, unless otherwise indicated.

Except where a solvent is cited, infrared light absorption spectra were determined on liquid films.

Nuclear magnetic resonance spectra were determined on solutions (ca. 10%) in carbon tetrachloride using tetramethylsilane as an internal standard. Most of the spectra phenylhydrazone which crystallised from ethanol and had m. p. 53-54° (lit.,<sup>51</sup> m. p. 54-55°; lit.,<sup>52</sup> m. p. 72-73°) (Found: C, 60.4; H, 7.15; N, 15.15%).

Electrolyses.<sup>17</sup>—These were carried out in a glass cell  $(39 \times 8 \text{ cm.})$  fitted with two spiral cooling coils, and immersed in an ice bath; in this way the temperature of the electrolyte was kept below 55°. The electrodes consisted of two platinum plates (6  $\times$  5 cm.), ca. 4 mm. apart, which were connected to a 110v d.c. supply. The electrical circuit also included a rheostat, an ammeter, and a commutator. At intervals during the electrolyses the direction of the current was reversed. Electrolyses were stopped when the electrolytes became slightly alkaline; at this stage there was often a noticeable drop in the current.

Chromatography.--Many of the products were purified

TABLE 3
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Oxidation of nerol and geraniol with manganese dioxide

				Proportions (%) of <i>cis</i> - and <i>trans</i> -aldehydes			
		Reaction	Approx. yield	From Nerol *		From Geraniol	
Manganese dioxide	Solvent	time	of aldehydes	cis	trans	cis	trans
Commercial <sup>a</sup>	CH <sub>2</sub> Cl <sub>2</sub>	60 hr.	60	75	<b>25</b>	35	<b>65</b>
Commercial (dried over P <sub>2</sub> O <sub>5</sub> )	CH <sub>2</sub> Cl <sub>2</sub>	120 hr.	80	70	30	35	<b>65</b>
Commercial (dried over $P_2O_5$ )	Acetone	48 hr.	60	60	40		
Commercial (dried over $P_2O_5$ )	Petroleum	48 hr.	60	60	40		
Alkaline <sup>b</sup>	Petroleum	43 hr.	80	<b>65</b>	<b>35</b>	<b>24</b>	76
Acidic <sup>e</sup>	Petroleum	1 week	10		—		-
Acidic	CHCl <sub>3</sub>	1 week	45	90	10	4	96

\* Contaminated with 3% geraniol.
\* B. C. L. Weedon and R. J. Woods, J. Chem. Soc., 1951, 2687. J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, J. Chem. Soc., 1952, 1094.
\* O. Mancera, G. Rosenkranz, and F. Sondheimer, J. Chem. Soc., 1953, 2189.

were run at 40 Mc./sec.; those quoted for the phytols, the geranylacetones, and the farnesoates were run on 60 Mc./sec. instruments which only became available when most of these studies had been completed.

Unless indicated to the contrary, optical rotations were determined on pure liquids (l = 1) in a standard polarimeter. Most of the measurements were made using a micro-tube because of shortage of material; the rotations cited are then the average of at least six readings and are probably accurate to  $\pm 0.02^{\circ}$ . It is not possible to place much reliance on comparisons of our rotations with those reported previously. Most of the latter were determined before gas-liquid (g.l.c.) chromatography had been introduced, and therefore the possibility that the samples used were contaminated with (optically active) impurities cannot always be excluded; thus both dextro-rotatory and optically inactive specimens of phytol have been reported.<sup>37</sup>

Starting Materials.—The natural phytol used in these studies was derived from grass meal chlorophyll and had  $\alpha_{\rm D}^{22\cdot 2}$  +0.03°; very little increase in the magnitude of rotation was observed at wavelengths down to  $300 \text{ m}\mu$ .

The citronellol  $(\alpha_{D}^{20.9} + 3.95^{\circ})$  was prepared by Ponndorf reduction of citronellal from Java citronella oil.

The cis- and trans-geranylacetones (Ib) were synthetic.<sup>21</sup> They readily separated from one another on g.l.c. (Apiezon T, 150°); their n.m.r. spectra are discussed in the theoretical section. The cis-ketone gave a 2,4-dinitrophenylhydrazone which crystallised from ethanol and had m. p. 64-65° (Found: C, 60.4; H, 7.0. C<sub>19</sub>H<sub>26</sub>N<sub>4</sub>O<sub>4</sub> requires C, 60.05; H, 7.0; N, 15.55%). The trans-ketone gave a 2,4-dinitroby chromatography on alumina (Peter Spence, type H, 100—200 mesh), using 2% ether in light petroleum (b. p. 40—60°) as eluant. A 5% solution of methyl acetate in light petroleum (b. p. 40-60°) followed by light petroleum alone, was percolated through columns of alumina before these were used to purify methyl or ether esters; this pretreatment was omitted in the isolation of terpene alcohols from their crude acetates. The course of a chromatogram was followed either by collecting arbitrary fractions of the eluate (e.g., every 100 ml.), evaporating these to dryness, and analysing the residues by g.l.c., or by monitoring the eluate with a dielectric-constant detector.53 The purity of all fractions was checked by g.l.c.

cis- and trans-Citrals (VIa).—(a) Samples of manganese dioxide (5-10 parts by weight) were added to solutions of nerol or geraniol (1-5 g.) in various solvents (ca. 20 vol.) at such a rate that the temperature did not exceed  $30^{\circ}$ . The mixtures were shaken at 20° in an atmosphere of nitrogen, and then filtered. The solid was washed well with ether, and the filtrate and washings were combined and evaporated. The products were analysed by n.m.r. spectroscopy (for cis- and trans-citral) and by g.l.c. (M.S. silicone 710 on celite, 180°; under these conditions the relevant compounds were all resolved, except for geraniol and cis-citral which gave 1 peak). The times of reaction, yields of aldehydes, and the proportions of cis- and transcitral, are summarised in Table 3.

(b) A sample of natural citral, and of citral synthesised from methyl-heptenone (Ia) by the method of Arens and

- <sup>50</sup> R. B. Woodward, Pure Appl. Chem., 1961, 2, 383.
   <sup>51</sup> D. W. Dicker and M. C. Whiting, J. Chem. Soc., 1958, 1994.
   <sup>52</sup> Y.-R. Naves, Helv. Chim. Acta, 1949, 32, 1801.
- 53 D. W. Turner, Nature, 1958, 181, 1265.

<sup>49</sup> L. M. Jackman, R. Rüegg, Cy. Ryser, C. von Planta, U. Gloor, H. Mayer, P. Schudel, M. Kofler, and O. Isler, Helv. Chim. Acta, 1965, 48, 1333.

van Dorp,<sup>54</sup> were both found to contain ca. 40% of the cisand ca. 60% of the trans-isomer (cf. Naves 55, 56).

3(RS), 7(R), 11(R), 15-Tetramethylhexadec-1-yn-3-ol.-

Ethylmagnesium bromide (from 5 g. of Mg) was prepared in ether (200 ml.). The ether was distilled off slowly whilst tetrahydrofuran (150 ml.) was added. The resulting solution was added slowly to tetrahydrofuran (80 ml.) through which acetylene was bubbled continuously. The passage of acetylene was continued for 1 hr. after the addition of the Grignard reagent. The resulting solution of ethynylmagnesium bromide 57 was cooled to  $0^{\circ}$  and 6(R), 10(R)-14-trimethylpentadecan-2-one (5.0 g., prepared from natural phytol) in tetrahydrofuran (15 ml.) was added. The mixture was stirred at  $20^{\circ}$  for 3 days, the complex was then decomposed by the addition of saturated aqueous ammonium chloride, and the product was isolated with ether. Distillation gave the acetylenic alcohol (3.9 g., 71%), b. p. 128- $132^{\circ}/0.35$  mm.,  $n_{\rm p}^{20}$  1.4578,  $d_4^{25}$  0.8482,  $\alpha_{\rm p}^{23\cdot2}$  +1.05°,  $[\alpha]_{\rm p}^{23\cdot2}$  +1.24°,  $\nu_{\rm max}$  3378, 3311, and 2128 cm.<sup>-1</sup> (no absorption the second se tion in the carbonyl region) (Found: C, 81.3; H, 13.1. Calc. for C<sub>20</sub>H<sub>38</sub>O: C, 81.55; H, 13.0%). Reaction with the Grignard reagent for one day gave a product contaminated with starting material. Reaction of the ketone with lithium acetylide in liquid ammonia also gave an impure product. Reaction of the ketone with sodium acetylide is unsatisfactory (cf. Fischer *et al.*<sup>4</sup>).

The partial reduction of the acetylenic alcohol to isophytol has been reported previously.4,6,12,14,58

Isomerisation of Isophytol (cf.4,6).-A mixture of acetic anhydride (2.0 g.) and  $(\pm)$ -isophytol (5.0 g.) was boiled under reflux for 17 hr., then cooled and poured into water. Isolation with ether in the usual way gave a mixture (5.0 g.) of phytyl acetates and phytadienes,  $\nu_{\rm max}$  1739, 1675, 1642, 1608, 1597, and 1232 cm.<sup>-1</sup>. Chromatography on alumina (27 imes 3 cm. column), using 2% ether in light petroleum (b. p. 40-60°) as eluant, resulted in complete hydrolysis of the acetates and gave (a) a mixture of phytadienes (2.0 g.) and (b) a mixture (2.2 g.) of cis- and transphytol,  $\nu_{max.}$  3413 and 1684 cm.<sup>-1</sup>; g.l.c. confirmed the presence of both isomers in comparable proportions.

Oxidation of Phytol.—(a) Natural phytol (10.0 g.) in methylene dichloride (100 ml.) was shaken with manganese dioxide (50 g., commercial) for 50 hr. in an atmosphere of nitrogen. The mixture was filtered and the solid was washed thoroughly with ether. The filtrate and washings were combined and evaporated. Distillation of the residue gave phytenal (5.5 g.), b. p. 159-162°/1 mm.,  $n_{\rm D}^{23\cdot5}$  1·468—1·470,  $\lambda_{\rm max}$  (CH<sub>2</sub>Cl<sub>2</sub>) 238 mµ ( $\varepsilon$  11,300),  $\nu_{\rm max}$  1678, 1631, and 1616 cm.<sup>-1</sup> (no absorption in the OH region), 7 7.88 (Found: C, 81.5; H, 13.15. Calc. for  $C_{20}H_{38}O$ : C, 81.55; H, 13.0%). G.l.c. showed the presence of low boiling impurities (possibly phytadienes). The semicarbazone crystallised from ethanol and had m. p. 119·5—120°,  $\lambda_{max}$  274 m $\mu$  ( $\epsilon$  29,800) (Found: C, 71·75; H, 11·55; N, 12·05. C<sub>21</sub>H<sub>41</sub>N<sub>3</sub>O requires C, 71·75; H, 11.75; N, 11.95%). The 2,4-dinitrophenylsemicarbazone crystallised from ethanol and had m. p. 106–108°,  $\lambda_{max}$ 267 and 320 mµ (z 27,500 and 19,000, respectively) (Found:

54 J. F. Arens and D. A. van Dorp, Rec. Trav. chim., 1948, 67, 973.

- 55 Y.-R. Naves, Bull. Soc. chim. France, 1958, 247, 687.
- <sup>56</sup> Y.-R. Naves, *Compt. rend.*, 1960, **251**, 900.
   <sup>57</sup> E. R. H. Jones, L. Skatteböl, and M. C. Whiting, *J. Chem.* Soc., 1956, 4765. <sup>58</sup> H. Lindlar, Helv. Chim. Acta, 1952, **35**, 446.

C, 62·4; H, 8·5; N, 13·8.  $C_{27}H_{43}N_5O_5$  requires C, 62·65; H, 8.35; N, 13.55%). A phytenal of unknown geometrical configuration was prepared by Karrer and Epprecht 59 from phytol via phytyl bromide.

(b) A mixture of cis- and trans-phytol (325 mg.) (prepared by isomerisation of isophytol) in methylene dichloride (7 ml.) was shaken with manganese dioxide (2.0 g.) for 50 hr. in an atmosphere of nitrogen. Isolation of the product as in the previous experiment gave a crude mixture of cis- and trans-phytenal (200 mg.),  $\nu_{max}$  1678 and 1629 cm.<sup>-1</sup>,  $\tau$  7.88 and 8.12.

Oxidation of Phytenal.-Sodium hydroxide (2.7 g.) in water (60 ml.) was added slowly (30 min.) to a stirred mixture of phytenal (5.3 g.) (prepared by oxidising natural phytol as described above), silver nitrate (7.6 g.), ethanol (130 ml.), and water (30 ml.). Water (60 ml.) was added, and the mixture was stirred for 16 hr. and then filtered. The ethanol was evaporated from the filtrate under reduced pressure, and the aqueous solution was extracted with light petroleum (b. p.  $40-60^{\circ}$ ). The aqueous solution was then acidified with hydrochloric acid, and the organic acid thus liberated was isolated with ether. The crude product ( $v_{max.}$  1686 and 1634 cm.<sup>-1</sup>) in ether was treated with a slight excess of diazomethane giving, after evaporation, crude methyl phytenoate (4·1 g.),  $\nu_{\rm max.}$  1718 and 1634 cm.-1,  $\tau$  7.89 ( $\beta$ -Me in *trans*-ester); g.l.c. showed the presence of two major components in the proportions of ca. 3:7. Chromatography on alumina revealed the presence of both cis-  $(\tau 8.14)$  and trans-methyl phytenoate  $(\tau 7.89)$ .

A phytenoic acid of unknown geometrical configuration has been prepared by oxidation of natural phytol with chromic acid.<sup>60</sup> Phytenoates, undoubtedly mixtures of cis- and trans-isomers, have been prepared from appropriate C<sub>18</sub>-ketones by Reformatsky reactions.<sup>9,10,61</sup>

cis- and trans-Methyl Geranates (IIIa).--Methoxyacetylene  $^{62}$  (7.15 g.) in ether (50 ml.) was added to a cooled  $(-70^{\circ})$  solution of ethylmagnesium bromide (from 3.05 g. of Mg) in ether (50 ml.). The mixture was allowed to warm to 20°, heated under reflux for 2 hr. using a cold  $(-40^\circ)$  condenser, and then cooled to  $0^\circ$ . 6-Methylhept-5-en-2-one (16.0 g.) in ether (20 ml.) was added, and the mixture was heated under reflux for 2.5 hr., stirred at 20° overnight, and then cooled to 0°. Ammonium chloride (28 g.) in water was added, and the crude product (20 g.)was isolated with ether (ca. 20% unreacted ketone was detected by g.l.c.).

Sulphuric acid (10 ml., 10% w/v) was added to the crude product in methanol (100 ml.). Heat was evolved; after 2 hr. the mixture was diluted with water, and the product was isolated with ether. Distillation gave the crude methyl geranates (14 g.), b. p. 65-100°/1 mm.; g.l.c. before and after distillation indicated the presence of roughly equal amounts of the two isomers, and ca. 10% of methyl heptenone. Chromatography on alumina gave: (a) cis-methyl geranate, b. p. 58°/0·4 mm.,  $n_{\rm D}^{22}$  1·4675,  $\lambda_{\rm max.}$  210—215 mµ ( $\epsilon$  12,500),  $v_{max}$  1712 and 1641 cm.<sup>-1</sup> (Found: C, 72.45; H, 9.95. Calc. for  $C_{11}H_{18}O_2$ : C, 72.5; H, 9.95%); (b) trans-methyl geranate, b. p.  $63^{\circ}/0.35$  mm.,  $n_{\rm D}^{22}$  1.4708,

- 60 R. Willstätter, E. W. Mayer, and E. Hüni, Annalen, 1911,
- **378**, 73. <sup>61</sup> P. Karrer, A. Epprecht, and H. König, *Helv. Chim. Acta*,
- <sup>62</sup> G. Eglinton, E. R. H. Jones, B. L. Shaw, and M. C. Whiting, J. Chem. Soc., 1954, 1860.

<sup>59</sup> P. Karrer and A. Epprecht, Helv. Chim. Acta, 1941, 24, 1039.

 $\lambda_{max.}$  218 mµ ( $\epsilon$  16,750),  $\nu_{max.}$  1712 and 1641 cm.  $^{-1}$  (Found: C, 72.4; H, 10.0%).

Nerol and Geraniol (Va).—(a) Lithium aluminium hydride (0.42 g.) in ether (15 ml.) was added slowly (30 min.) to a cold (ca.  $-20^{\circ}$ ) solution of cis-methyl geranate (1.35 g.) in ether (6 ml.). After 10 min., methyl acetate was added (to decompose the excess of hydride) followed by a saturated solution of ammonium chloride (3 g.). Isolation with ether gave a product (1.1 g.) which was shown by g.l.c. to contain ca. 5% of an impurity (probably neryl acetate). Distillation through a micro-spinning band column gave nerol, b. p. 70°/0.5 mm.,  $n_{D}^{24}$  1.4720 (Found: C, 77.8; H, 11.55. Calc. for C<sub>10</sub>H<sub>18</sub>O: C, 77.85; H, 11.75%). The i.r. spectrum was identical with that of authentic nerol. On g.l.c. of mixtures, the synthetic alcohol separated from geraniol, but not from authentic nerol. The tetrabromide had m. p. 117—118° (lit.,<sup>63</sup> m. p. 116—118°) undepressed on admixture with an authentic specimen.

(b) Similar reduction of *trans*-methyl geranate (1.65 g.) gave a crude product containing *ca*. 5% of an impurity. Purification *via* the calcium chloride adduct gave geraniol, b. p. 70°/0.4 mm.,  $n_{\rm D}^{22}$  1.4742 (Found: C, 77.65; H, 11.6%). The product did not separate from authentic geraniol on mixed g.l.c.; the two samples had identical i.r. spectra. The diphenylurethane had m. p. 80–81.5°, undepressed on admixture with an authentic specimen (lit.,<sup>64</sup> m. p. 82°).

The Methyl Farnesoates (IIIb).-(a) cis-Geranylacetone (7.0 g.) in ether (15 ml.) was added to a suspension of methoxyacetylenylmagnesium bromide (from 1.9 g. of Mg). The mixture was stirred under reflux overnight and then cooled  $(0^{\circ})$ . Decomposition of the complex, and isolation of the product in the usual way, gave an oil (7.5 g.) which, in methanol (50 ml.), was treated with sulphuric acid (20 ml., 10% w/v). The mixture was warmed (40-50°) for 2 hr., then cooled and diluted with water (100 ml.). Isolation with ether gave a crude product (5.0 g.) which was shown by g.l.c. to contain roughly equal amounts of two isomeric farnesoates and ca. 2% of cis-geranylacetone. Distillation gave the esters, b. p. 110-112°/0.5 mm.,  $n_{\rm p}^{23}$  1·4815,  $\lambda_{\rm max}$  217 mµ ( $\epsilon$  13,500),  $v_{\rm max}$  1718 and 1645 cm.<sup>-1</sup> (Found: C, 77·00; H, 10·35. Calc. for C<sub>16</sub>H<sub>26</sub>O<sub>2</sub>: C, 76.75; H, 10.45%). Chromatography of the mixture of esters (2.0 g.) gave: (i) cis-2, cis-6-methyl farnesoate (0.70 g.), b. p. 125—127°/3 mm.,  $n_{\rm p}^{26}$  1·4795,  $\lambda_{\rm max}$  210 mµ ( $\varepsilon$  12,500),  $\nu_{\rm max}$  1718 and 1647 cm.<sup>-1</sup> (Found: C, 77·2; H, 10·5.  $C_{16}H_{26}O_2$  requires C, 76.75; H, 10.45%): (ii) trans-2,cis-6methyl farnesoate (0.60 g.), b. p. 130–133°/3 mm.,  $n_{\rm p}^{25}$ 1.4813,  $\lambda_{max.}$  210 mµ ( $\epsilon$  14,500),  $\nu_{max.}$  1718 and 1647 cm.<sup>-1</sup> (Found: C, 77.2; H, 10.5%).

(b) trans-Geranylacetone (5.0 g.) was similarly converted into a mixture (4.5 g.) of farnesoates (containing 2% of starting material), b. p. 110°/0.4 mm. Chromatography of the mixture (2.7 g.) gave: (i) cis-2,trans-6-methyl farnesoate (0.9 g.), b. p. 130—133°/3 mm.,  $n_{\rm p}^{21}$  1.4826,  $\lambda_{\rm max}$ . 210 mµ ( $\varepsilon$  13,500),  $v_{\rm max}$  1718 and 1647 cm.<sup>-1</sup> (Found: C, 76.95; H, 10.5%); (ii) trans-2,trans-6-methyl farnesoate (0.85 g.), b. p. 133—135°/3 mm.,  $n_{\rm p}^{22}$  1.4840,  $\lambda_{\rm max}$  210 mµ ( $\varepsilon$  14,000),  $v_{\rm max}$ . 1718 and 1647 cm.<sup>-1</sup> (Found: C, 77.05 H, 10.5%).

Each of the four methyl farnesoates gave only one peak on g.l.c. The relative retention times of the four isomers on poly(ethylene glycol succinate)  $(172^{\circ})$  were 0.60: 0.90: 0.75:1.00, and on Apiezon T (200°) were 0.70: 0.90: 0.82: 1.00, respectively (Figure 2).

The Farnesols (Vb).-(a) cis-2, cis-6-Methyl farnesoate

(0.30 g.) in ether (10 ml.) was added to a cold  $(-60^{\circ})$  suspension of lithium aluminium hydride (0.10 g.) in ether (10 ml.). The mixture was stirred at  $-30^{\circ}$  for 4 hr., and the excess of hydride was then decomposed by the addition of wet ether. Saturated ammonium chloride solution (2 ml.) was added and the product was isolated with ether to give *cis*-2,*cis*-6-farnesol (0.26 g.), b. p. 127°/3 mm.,  $n_{\rm p}^{20}$  1.4850,  $\nu_{\rm max}$ . 3333 and 1667 cm.<sup>-1</sup> (Found: C, 81.3; H, 11.65. Calc. for C<sub>15</sub>H<sub>26</sub>O: C, 81.0; H, 11.8%).

(b) Similarly reduction of the *trans*-2,*cis*-6-ester (0.20 g.) gave *trans*-2,*cis*-6-farnesol (0.16 g.) b. p.  $132^{\circ}/3$  mm.,  $n_{\rm D}^{-3}$  1.4851,  $\nu_{\rm max}$ . 3322 and 1667 cm.<sup>-1</sup> (Found: C, 81.15; H,  $12.0^{\circ}_{\odot}$ ).

(c) Reduction of the cis-2,trans-6-ester (0.20 g.) gave cis-2,trans-6-farnesol (0.16 g.), b. p.  $135^{\circ}/3$  mm.,  $n_{\rm D}^{25}$ 



Retention time

FIGURE 2 Gas-liquid chromatogram of the methyl farnesoates on poly(ethylene glycol succinate) (6 ft. column, 172°)

1.4850,  $\nu_{max.}$  3333 and 1667 cm.  $^{-1}$  (Found: C, 81.6; H, 11.85%).

(d) Reduction of the trans-2,trans-6-ester (0.25 g.) gave trans-2,trans-6-farnesol (0.20 g.), b. p. 137°/3 mm.,  $n_{\rm D}^{22}$  1.4870,  $\nu_{\rm max}$  3333 and 1667 cm.<sup>-1</sup> (Found: C, 80.85; H, 11.85%). The hydrogen 3-nitrophthalate had m. p. 93—94°, undepressed on admixture with an authentic specimen (lit.,<sup>65</sup> m. p. 93—93.5°).

Each of the four farnesols gave only one peak on g.l.c. The relative retention times of the four isomers on poly(ethylene glycol succinate)  $(172^\circ)$  were 0.76: 0.92: 0.87: 1.00, on poly(ethylene glycol adipate)  $(150^\circ) 0.74: 0.91: 0.86: 1.00$ , and on Apiezon T  $(200^\circ) 0.75: 0.86: 0.86: 1.00$ , respectively.

cis- and trans-Methyl Phytenoate (IIIc).—6(R),10(R),14-Trimethylpentadecan-2-one (10.0 g.) was reacted with methoxyacetylenylmagnesium bromide (from 2.2 g. of Mg), in the manner described above for methylheptenone. Sulphuric acid (6 ml., 10% w/v) was added to the crude product (10.2 g.) in methanol (80 ml.), followed by sufficient ether (ca. 30 ml.) to give a homogeneous solution. After

<sup>63</sup> H. von Soden and W. Treff, Ber., 1906, **39**, 906.

<sup>64</sup> H. Erdmann and P. Huth, J. prakt. Chem., 1896, 53, 45; 1897, 56, 28.

65 T. Lennatz, Chem. Ber., 1943, 76, 831.



16 hr., water was added and the product (9.3 g.) was isolated with ether. G.l.c. indicated the presence of both esters in roughly equal amounts, and *ca.* 3% of unchanged starting material. Chromatography of the mixture on alumina gave: (a) cis-methyl phytenoate, b. p. 149—152°/ 0.5 mm.,  $n_D^{21}$  1.4588,  $d_4^{25}$  0.8694,  $\alpha_D^{22}$  +0.86°,  $[\alpha]_D^{22}$  +0.99°,  $\lambda_{\text{max}}$  220 mµ ( $\varepsilon$  14,400),  $\nu_{\text{max}}$  1715 and 1645 cm.<sup>-1</sup> (Found: C, 77.85; H, 12.4. C<sub>21</sub>H<sub>40</sub>O<sub>2</sub> requires C, 77.7; H, 12.4%): (b) trans-methyl phytenoate, b. p. 157—158°/0.6 mm.,  $n_D^{27.5}$  1.4588,  $d_4^{25}$  0.8750,  $\alpha_D^{20.9}$  —0.97°,  $[\alpha]_D^{20.9}$  —1.11°,  $\lambda_{\text{max}}$  219 mµ ( $\varepsilon$  16,200),  $\nu_{\text{max}}$  1715 and 1645 cm.<sup>-1</sup> (Found: C, 77.9; H, 12.65%).

4-E thoxy carbonyl-3-methylbut-3-ene-1-carboxylicAcid (VII) .--- This half ester was prepared by the method of Linstead et al.<sup>30</sup> Esterification of a small sample with diazoethane gave the diethyl ester, b. p. 87-88.5°/0.6 mm.,  $n_{\rm D}^{22\cdot5}$  1·4452,  $\lambda_{\rm max}$  216 mµ ( $\varepsilon$  14,300),  $\nu_{\rm max}$  1733, 1712, and 1647 cm.<sup>-1</sup> (Found: C, 61·7; H, 8·25. C<sub>11</sub>H<sub>18</sub>O<sub>4</sub> requires C, 61·65; H, 8·45%). The relative intensities of the  $\beta$ -methyl bands ( $\tau$  8.09 and 7.85) in the n.m.r. spectrum indicated that the ester consisted of ca. 70% of the cisand ca. 30% of the trans-isomer. Attempts to change this proportion, by ultraviolet irradiation of the ester in boiling benzene in the presence of iodine for 8 hr., were unsuccessful. cis- and trans-Ethyl 7(RS), 11(R')-Phytenoate (XVIII, R = Et).—The preceding half ester (23 g.) and 3(RS),-11(R'), 15-trimethyldodecanoic acid (5.0 g.) were added to a solution of sodium methoxide (from 0.1 g. of Na) in methanol (250 ml.), and the solution was electrolysed (3-4 amp). The solvent was evaporated under reduced pressure, and the residue was dissolved in ether. The solution was washed with 2% aqueous sodium hydroxide, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated. Chromatography of the crude product gave: (a) the cis-ethyl ester (0.9 g.),  $v_{max}$ . 1715 and 1645 cm.<sup>-1</sup> (Found: C, 77.85; H, 12.75. Calc. for  $C_{22}H_{42}O_2$ : C, 78.05; H, 12.5%); (b) the trans-ethyl ester (0.22 g.)  $\nu_{max.}$  1721 and 1650 cm.  $^{-1}$  (Found: C, 78.0; H, 12.55%).

cis- and trans-Phytol (Vc).—(a) A suspension of lithium aluminium hydride (88 mg.) in ether (5 ml.) was added slowly to a cooled (ca.  $-20^{\circ}$ ) solution of cis-methyl phytenoate (500 mg.) in ether (5 ml.), and the mixture was stirred at 0° for 10 min. Methyl acetate (1 ml.) was added (to decompose the excess of hydride) followed by a saturated solution of ammonium chloride (1 g.). Isolation with ether gave a crude product (500 mg.) which was shown (i.r. spectroscopy) to be contaminated with 5—10% of phytyl acetate. Chromatography on a short column of alumina (15 × 1.5 cm.), and evaporation under reduced pressure (0.05 mm., 2 hr.) gave cis-phytol (340 mg.),  $v_{max}$ . 3226 and 1661 cm.<sup>-1</sup> (Found: C, 80.7; H, 13.65. C<sub>20</sub>H<sub>40</sub>O requires C, 81.0; H, 13.6%).

(b) A similar reduction of the *trans*-ester (993 mg.) gave *trans*-phytol (760 mg.)  $\nu_{max}$ . 3226 and 1661 cm.<sup>-1</sup> (Found: C, 80.95; H, 13.6%). In mixed gas-liquid chromatograms on poly(ethylene glycol succinate) at 150°, the *trans*-alcohol separated from the *cis*-alcohol, but not from natural phytol. The relative retention times of the *cis*- and *trans*-alcohols were 0.88: 1.0.

(c) Reduction of cis-ethyl 7(RS),11(R')-phytenoate (877 mg.) gave the corresponding cis-alcohol (790 mg.) (Found: C, 80.4; H, 13.65%).

(d) Reduction of trans-ethyl 7(RS), 11(R')-phytenoate (217 mg.) gave the corresponding trans-alcohol (180 mg.) (Found: C, 80.65; H, 13.95%). In mixed gas-liquid

chromatograms on poly(ethylene glycol succinate) it separated from the *cis*-phytols, but not from natural phytol.

 $\beta$ -Methylglutaric Half Esters (IX).—The methyl half ester was prepared from  $\beta$ -methylglutaric anhydride, and resolved into its (+)-R and (-)-S enantiomorphs, as described by Linstead *et al.*<sup>39</sup>

β-Methylglutaric anhydride (50 g.) was added to a solution of benzyloxysodium (from 9.0 g. of Na) in benzyl alcohol (250 ml.); heat was evolved. The mixture was kept for 1 hr. and then poured into water (500 ml.). The excess of benzyl alcohol was extracted with ether. The aqueous residue was acidified with a slight excess of 2N-hydrochloric acid, and the product was isolated with ether. Distillation gave benzyl hydrogen β-methylglutarate (47 g., 51%), b. p. 160—163°/0·7 mm.,  $n_{\rm D}^{\rm 31}$  1·5048,  $v_{\rm max}$  1736 and 1712 cm.<sup>-1</sup> (Found: C, 66·45; H, 7·0%; Equiv., 234. C<sub>13</sub>H<sub>16</sub>O<sub>4</sub> requires C, 66·1; H, 6·85%; Equiv., 236).

(+)-Methyl 3(R),7-Dimethyloctanoate (XI).—4-Methylpent-2-enoic acid ( $v_{max}$ . 1692 and 1645 cm.<sup>-1</sup>) was prepared from isobutyraldehyde (shown by g.l.c. to contain none of the n-isomer) and malonic acid by the method of Goldberg and Linstead,<sup>66</sup> and reduced in alcohol with hydrogen and Adams catalyst to 4-methylpentanoic acid,  $v_{max}$ . 1709 cm.<sup>-1</sup>.

A mixture of 4-methylpentanoic acid (45 g.) and (+)-*R*-methyl hydrogen  $\beta$ -methylglutarate (5.76 g.) was added to a solution of sodium methoxide (from 0.2 g. of Na) in methanol (300 ml.), and the solution was electrolysed (4 amp., 5.5 hr.). The solvent was evaporated under reduced pressure, and the residue was dissolved in ether. The solution was washed with 2% aqueous sodium hydroxide, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated. Chromatography of the residue (9 g.) gave the *ester* (3.0 g., 45% based on half ester), b. p. 53°/0.5 mm.,  $n_{\rm D}^{24}$  1.4230,  $d_4^{24}$  0.8594,  $\alpha_{\rm D}^{22.6}$  +3.66°, [ $\alpha$ ]<sub>D</sub><sup>22.6</sup> +4.26°,  $\nu_{\rm max}$  1739 cm.<sup>-1</sup> (Found: C, 71.15; H, 11.95. C<sub>11</sub>H<sub>22</sub>O<sub>2</sub> requires C, 70.9; H, 11.9%). The products of symmetrical anoidic coupling were not purified.

The 3,7-Dimethyloctanols (XII).—(a) The preceding ester (1.9 g.) in ether (10 ml.) was added slowly to a suspension of lithium aluminium hydride (1.0 g.) in ether (50 ml.). The mixture was stirred for 30 min. and then sulphuric acid (40 ml., 10% w/v) was added to decompose the excess of hydride. Isolation with ether and distillation gave 3(R),7-dimethyloctanol (1.5 g.), b. p. 92°/0.4 mm.,  $n_{\rm p}^{23.5}$  1.4348,  $d_4^{25}$  0.8235,  $\alpha_{\rm p}^{22.5}$  +4.30°, [a]<sub>p</sub><sup>22.5</sup> +5.23°,  $v_{\rm max}$  3333 cm.<sup>-1</sup> (Found: C, 75.8; H, 14.0. Calc. for C<sub>10</sub>H<sub>22</sub>O: C, 75.9; H, 14.0%). Only one peak was observed on g.l.c.

(b) A solution of (+)-citronellol (320 g.) in ethyl acetate (600 ml.) was shaken with palladised strontium carbonate (2 g., ca. 5% Pd) in hydrogen (at 100 atmospheres) at 70° for 1 hr., and then at 20° for 16 hr. Removal of catalyst and solvent, and distillation gave 3(R'),7-dimethyloctanol (311 g.), b. p. 105—106°/10 mm.,  $n_{\rm D}^{23}$  1·4361,  $d_4^{23}$  0·8271,  $\alpha_{\rm D}^{26\cdot 1}$  +3·77°,  $[\alpha]_{\rm D}^{26}$  +4·56°,  $\nu_{\rm max}$  3333 cm.<sup>-1</sup> (lit.,67 gives b. p. 81—82°/2·6 mm.,  $n_{\rm D}^{20}$  1·4352,  $d_4^{20}$  0·8302,  $[\alpha]_{\rm D}^{20}$  +5·18°; g.l.c. not reported). Only one peak was observed on g.l.c., and there was no separation in a mixed chromatogram with the alcohol from (a). There was no absorption when a sample of the alcohol, in glacial acetic acid, was shaken in hydrogen in the presence of a large excess of Adams catalyst.

(-)-4(R'),8-Dimethylnonanoic Acid (XIII).—A mixture of 3(R'),7-dimethyloctanol (311 g.), hydrobromic acid

<sup>66</sup> A. A. Goldberg and R. P. Linstead, J. Chem. Soc., 1928, 2343.

<sup>67</sup> Y.-R. Naves, Helv. Chim. Acta, 1946, 29, 1447.

(925 ml., 45%), and concentrated sulphuric acid (125 ml.) was boiled under reflux for 8 hr., and then cooled. The bromide layer was separated, washed with concentrated sulphuric acid, then with aqueous methanolic ammonia and finally with water, and dried (Na<sub>2</sub>SO<sub>4</sub>). Distillation gave the crude bromide (360 g.), b. p. 83-84°/4 mm.,  $n_{\rm D}^{22}$  1·4562,  $\alpha_{\rm D}^{21\cdot8}$  –4·80°, which was contaminated with the starting material. In a smaller scale experiment the product had  $n_{\rm D}^{21\cdot5}$  1·4562,  $d_4^{23}$  1·064,  $\alpha_{\rm D}^{22\cdot5}$  – 5·04°,  $[\alpha]_{\rm D}^{22\cdot5}$  – 4·74° (lit.,<sup>68</sup> b. p. 102—107°/15 mm.,  $d_4^{20}$  1·05,  $[\alpha]_{\rm D}^{20}$  $-4.6^{\circ}$ ).

The crude bromide (360 g.) was added to a solution of potassium cyanide (180 g.) in water (420 ml.) and methanol (850 ml.), and the mixture was stirred under reflux for 1 week. The methanol was distilled off through a Dufton column (12  $\times$  1 in.). The residue was cooled, and the product was isolated with ether. Distillation gave the crude nitrile (240 g.), b. p. 96—103°/7 mm.,  $\alpha_D^{21\cdot6} + 1\cdot97^\circ$ .

The crude nitrile (240 g.) was added to a solution of potassium hydroxide (135 g.) in water (1350 ml.) and ethanol (650 ml.), and the mixture was boiled under reflux for 1 week. The ethanol was distilled off through a Dufton  $\operatorname{column}(12 \times 1 \text{ in.})$ , the residue was cooled, and the neutral material was extracted with ether. The aqueous solution was acidified with concentrated hydrochloric acid, and the organic acid thus liberated was isolated with ether. Distillation gave 4(R'),8-dimethylnonanoic acid (161 g.), b. p.  $136-139^{\circ}/4\cdot5$  mm.,  $n_{\rm D}^{20}$   $1\cdot4392$ ,  $d_4^{21}$   $0\cdot8925$ ,  $\alpha_{\rm D}^{20\cdot8}$  $-0\cdot48^{\circ}$ ,  $[\alpha]_{\rm D}^{20\cdot8}$   $-0\cdot54^{\circ}$  (lit.,<sup>68</sup>  $[\alpha]_{\rm D}^{17}$   $-1\cdot0^{\circ}$  for the acid prepared from dihydrocitronellol  $[\alpha]_{\rm D}$  +3·5°, and lit.,<sup>69</sup>  $[\alpha]_p - 0.58^\circ$  for the acid prepared from dihydrocitronellol  $[\alpha]_{\rm p}$  +2·38°). Recycling the low-boiling fractions, and the neutral fraction from the hydrolysis, gave more of the dimethylnonanoic acid (35 g.) and dihydrocitronellol (30 g.). The tribromanilide crystallised from alcohol in plates, m. p. 84.5-85° (Found: C, 41.35; H, 5.0; N, 3.05. Calc. for C<sub>17</sub>H<sub>24</sub>Br<sub>3</sub>NO: C, 41.0; H, 4.85; N, 2.8%) (lit.,<sup>70</sup> m. p. 85°).

The 3,7,11-Trimethyldodecanoic Acids (XIV).-(a) The preceding acid (73.7 g.) and ( $\pm$ )-benzyl hydrogen  $\beta$ -methylglutarate (191 g.) were added to a solution of sodium methoxide (from 1.4 g. of Na) in methanol (1600 ml.). The mixture was electrolysed (4 amp.) in portions until each became slightly alkaline. The solutions were combined and evaporated under reduced pressure. The residue in ether was washed with 2% sodium hydroxide, and dried  $(Na_2SO_4)$ . Distillation gave crude benzyl 3(RS),7(R'),11trimethyldodecanoate (50 g., 28%), b. p. 182-198°/1·0 mm.,  $n_n^{20}$  1.4827—1.4905. A mixture of the crude ester and sodium hydroxide (50 g.) in water (50 ml.) and methanol (200 ml.) was boiled under reflux for 16 hr. Isolation of the product in the usual way gave 3(RS),7(R'),11-trimethyldodecanoic acid (27 g.), b. p. 146—148°/0·9 mm.,  $n_{\rm p}^{18\cdot5}$ 1·4470,  $d_4^{22}$  0·8831,  $\alpha_{\rm p}^{22\cdot1}$  —0·08°,  $[\alpha]_{\rm p}^{22\cdot1}$  —0·10° (Found: C, 74·45; H, 12·55. C<sub>15</sub>H<sub>30</sub>O<sub>2</sub> requires C, 74·3; H, 12·5%). The tribromoanilide crystallised from methanol and had m. p. 76-77°. The methyl ester gave only one peak on g.l.c. The acid can also be prepared from the  $(\pm)$ -methyl half ester, but chromatography must then be used to separate the methyl ester of the desired product.

(b) A solution of S-methyl hydrogen  $\beta$ -methylglutarate (10.0 g.) and 4(R'),8-dimethylnonanoic acid (37 g.) in methanol (250 ml.) containing sodium methoxide (from 0.05 g. of Na) was electrolysed. Isolation of the crude product (37 g.), and chromatography on alumina ( $65 \times 3.5$  cm. column), gave the 3(S),7(R')-methyl ester (3.0 g.), b. p. 105—106°/0.4 mm.,  $n_{\rm D}^{19.5}$  1.4379,  $d_4^{23}$  0.8904,  $\alpha_{\rm D}^{22.2}$  -3.12°, 
$$\label{eq:alpha} \begin{split} [\alpha]_D{}^{2\cdot 22} &= 3\cdot 51^\circ, \nu_{max}. 1736 \ \text{cm.}{}^{-1} \ (\text{Found: C, } 74\cdot 85; \ \text{H, } 12\cdot 45. \\ C_{16} H_{32} O_2 \ \text{requires C, } 75\cdot 0; \ \text{H, } 12\cdot 6\%). \\ \end{split}$$
ing the ester (ca. 8g.) contaminated with small amounts of the symmetrical products of anodic coupling were also obtained, but not purified. Hydrolysis of the (pure) methyl ester (2.9 g.) with aqueous methanolic potassium hydroxide gave 3(S),7(R'),11-trimethyldodecanoic acid (2.5 g.), b. p. 141—142°/0.7 mm.,  $n_{\rm D}^{26\cdot5}$  1.4429,  $d_4^{27}$  0.8760,  $\alpha_{\rm D}^{24}$  -3.98°,  $[\alpha]_{D}^{24} - 4.55^{\circ}, \nu_{max}, 1704 \text{ cm.}^{-1} (\text{Found: C, } 74.24; \text{ H, } 12.35\%).$ Hydrolysis of the crude ester (8 g.) gave the same acid (6.2 g.) contaminated with small amounts of  $\beta\beta'$ -dimethylsuberic acid.

(c) A solution of R-methyl hydrogen  $\beta$ -methylglutarate (5.5 g.) and 4(R'),8-dimethylnonanoic acid (20.0 g.) in methanol (260 ml.) containing sodium methoxide (from 0.05 g. of Na) was electrolysed (2 amp., 110 volts). Isolation of the crude product (18.5 g.) and chromatography in the usual way gave: (i) 2,6(S'),11(S'),15-Tetramethylhexadecane, b. p. 128—130°/0·5 mm.,  $n_{\rm D}^{23}$  1·4391,  $d_4^{22\cdot5}$ 0.7845,  $\alpha_D^{22\cdot3} = 0.25^{\circ}$ ,  $[\alpha]_D^{22\cdot3} = 0.31^{\circ}$ ; only one peak was observed on g.l.c. (ii) The 3(R), 7(R')-methyl ester (3.8 g., 43%), b. p. 107–109°/0.5 mm.,  $n_{\rm D}^{22}$  1.4361,  $\alpha_{\rm D}^{21.6}$  $+3.06^{\circ}$ ,  $\nu_{max}$  1739 cm.<sup>-1</sup> (Found: C, 75.2; H,  $12.85^{\circ}$ ). Only one peak was observed on g.l.c. Hydrolysis of the ester (3.7 g.) with aqueous methanolic potassium hydroxide gave 3(R),7(R'),11-trimethyldodecanoic acid (2.0 g.), b. p.  $\begin{array}{l} 139 - 142^{\circ}/0.6 \text{ mm., } n_{\rm D}^{25} \ 1.4424, \ d_4^{29} \ 0.8768, \ \alpha_{\rm D}^{27\cdot5} + 4\cdot06^{\circ}, \\ [\alpha]_{\rm D}^{27\cdot5} + 4\cdot56^{\circ}, \ \nu_{\rm max.} \ 1706 \ {\rm cm.}^{-1} \ ({\rm Found: C, 74\cdot3; H, 12\cdot35\%}). \\ The \ 6,10,14\text{-} Trimethylpentadecan-2-ones} \quad ({\rm XVI} \equiv {\rm Ic}).- \end{array}$ 

(a) Laevulic acid (50 g.) and 3(RS),7(R'),11-trimethyldodecanoic acid (3.0 g.) were added to a solution of sodium methoxide (from 0.10 g. of Na) in methanol (300 ml.), and the solution was electrolysed (3 amp.). Isolation of the crude product (16 g.) and chromatography gave 6(RS),-10(R'),14-trimethylpentadecan-2-one (1.0 g.),  $\alpha_{\rm p}^{23.6} - 0.20^{\circ}$ ,  $v_{max}$  1709 cm.<sup>-1</sup> (Found: C, 80.75; H, 13.4. Calc. for C<sub>18</sub>H<sub>36</sub>O: C, 80.5; H, 13.5%). A trace (<0.5%) of an impurity was detected by g.l.c. (lit.,  $^{6}$   $\alpha_{\rm p}$   $-0.24^{\circ}$  for the ketone prepared by a different route from (+)-citronellol). The semicarbazone crystallised from methanol at  $-15^{\circ}$ in plates, m. p. 67-67.3° (Found: C, 70.75; H, 11.65; N, 12.9. Calc. for  $C_{19}H_{39}ON_3$ : C, 70.1; H, 12.1; N, 12.9%) (lit.,<sup>6</sup> m. p. 68°). The 2,4-dinitrophenylsemicarbazone crystallised from ethanol and had m. p. 177-178° (Found: N, 14.35.  $C_{25}H_{41}O_5N_5$  requires N, 14.25%).

(b) Laevulic acid (100 g.) and 3(S),7(R'),11-trimethyldodecanoic acid (6.2 g., containing a small amount of  $\beta$ ,  $\beta$ '-dimethylsuberic acid) were added to sodium methoxide (from 0.2 g. of Na) in methanol (350 ml.), and the solution was electrolysed (3.5-4 amp.). Isolation of the crude product and chromatography gave 6(S), 10(R'), 14-trimethylpentadecan-2-one (1·2 g.),  $n_{\rm D}^{23}$  1·4431,  $d_4^{28}$  0·8294,  $\alpha_{\rm D}^{22\cdot7} = -0.98^{\circ}$ ,  $[\alpha]_{\rm D}^{22\cdot7} = 1.18^{\circ}$ ,  $\nu_{\rm max}$  1709 cm.<sup>-1</sup> (Found: C, 80.35; H, 13.65%). A trace (<0.5%) of an impurity was detected by g.l.c. The o.r.d. curve of the ketone in methanol showed a trough at 303 mµ,  $[\alpha] = -11.5^{\circ}$ , and a peak at 263 mµ,  $[\alpha] = +13 \cdot 0^{\circ}$ .

(c) Laevulic acid (70 g.) and 3(R), 7(R'), 11-trimethyldodecanoic acid (1.9 g.) were added to sodium methoxide (from 0.1 g. of Na) in methanol (300 ml.), and the solution

- <sup>68</sup> P. C. Jocelyn and N. Polgar, J. Chem. Soc., 1953, 132.
   <sup>69</sup> J. von Braun and W. Kaiser, Ber., 1923, 56, 2268.
   <sup>70</sup> N. Polgar and R. Robinson, J. Chem. Soc., 1945, 389.

was electrolysed. Isolation of the product in the usual way gave 6(R), 10(R'), 14-trimethylpentadecan-2-one (570 mg.),  $n_{\rm D}^{23}$  1·4430,  $d_4^{24}$  0·8324,  $\alpha_{\rm D}^{24\cdot6}$  + 0·65°,  $[\alpha]_{\rm D}^{24\cdot6}$  + 0·78°,  $\nu_{\rm max}$ , 1717 cm.<sup>-1</sup> (Found: C, 80·25; H, 13·55%). A trace (ca. 1%) of an impurity was detected by g.l.c. The o.r.d. curve of the ketone in methanol showed a peak at 303 mµ,  $[\alpha] = +11\cdot0^\circ$ , and a trough at 263 mµ,  $[\alpha] = -13\cdot0^\circ$ .

(d)<sup>24</sup> A stream of ozonised oxygen was passed into a cooled  $(0^{\circ})$  solution of (natural) phytol (60 g.) in acetic acid (70 ml.) and methyl acetate (15 ml.) until absorption of ozone ceased. The methyl acetate was evaporated under reduced pressure, and hydrogen peroxide (20 ml., 100 vol.) was added. The mixture was kept at 35° for 48 hr., and then poured into water. Isolation of the product with ether gave the crude ketone (27.5 g., 43%), b. p. 118-122°/ 0.4 mm.,  $n_{\rm D}^{22}$  1.4435—1.4450, which was shown by g.l.c. to contain 5-10% of an impurity (probably an aldehyde derived from phytadiene). The semicarbazone crystallised from methanol at  $-15^{\circ}$  in plates, m. p. 67–68°,  $[\alpha]_{\rm p}^{22\cdot 2}$  $-1.43^{\circ}$  (8% solution in MeOH) (Found: C, 70.4; H, 12.05; N, 13.0%) (lit.,<sup>28</sup> gives m. p. 66-67°). The m. p. of the semicarbazone was undepressed on admixture with the derivative of the ketone from (a). A mixture of the semicarbazone (4.5 g.) and 3N-sulphuric acid (60 ml.) was heated under reflux for 3 hr. and then cooled. The product was isolated with ether and distilled to give 6(R), 10(R), 14-trimethylpentadecan-2-one (2.8 g., 75%), b. p. 123-126°/ 0.25 mm,  $n_{\rm p}^{23}$  1.4430,  $d_4^{24}$  0.8328,  $\alpha_{\rm p}^{24\cdot 2}$  +0.58°,  $[\alpha]_{\rm p}^{24\cdot 2}$  +0.70°,  $v_{\rm max}$  1709 cm.<sup>-1</sup> (Found: C, 80.25; H, 13.7%). (Karrer *et al.*<sup>32</sup> give  $\alpha_{\rm D} + 0.22^{\circ}$ ). Only one peak was observed on g.l.c.; mixtures with the ketones prepared from (a), (b), and (c) did not separate on g.l.c. The 2,4-dinitrophenylsemicarbazone crystallised from ethanol and had m. p. 181.5-182° (Found: N, 14.0%). It did not depress the m. p. of the corresponding derivative of the ketone from (a).

The 2,6,10,14-Tetramethylpentadecanes (XVII).—(a) A solution of 6(RS),10(R'),14-trimethylpentadecan-2-one (1.02 g.) in tetrahydrofuran (10 ml.) was added to an excess (ca. 3 mol.) of methylenetriphenylphosphoran, prepared by adding ethereal butyl-lithium to a suspension of methyl-

triphenylphosphonium bromide (6 mol.) in tetrahydrofuran (120 ml.). The mixture was stirred for 30 min., and the excess of Wittig reagent was decomposed by the addition of acetone. Water was added, and the product was isolated in the usual way. Chromatography gave the tetramethylpentadecene (850 mg., 85%),  $\alpha_{\rm D}^{26\cdot1} - 0.15^{\circ}$ ,  $\nu_{\rm max}$ . 1642 and 885 cm.<sup>-1</sup>. Hydrogenation of the olefin in methyl acetate (10 ml.) over Adams catalyst (50 mg.), and removal of catalyst and solvent, gave 2,6(*RS*),10(*R'*),14tetramethylpentadecane (850 mg.),  $\alpha_{\rm D}^{25\cdot8} - 0.18^{\circ}$  (Found: C, 85·15; H, 14·9.  $C_{19}H_{40}$  requires C, 85·0; H, 15·0%). It exhibited no i.r. absorption bands attributable to olefinic impurities. The presence of *ca*. 1% of a more volatile hydrocarbon (probably 2,7,11-trimethyldodecane) was detected by g.l.c.

(b) Similarly 6(R), 10(R), 14-trimethylpentadecan-2-one (1·3 g., regenerated from the semicarbazone) was converted into the corresponding tetramethylpentadecene (1·15 g., 89%),  $\alpha_{\rm p}^{24\cdot3}$  0°,  $\nu_{\rm max}$ , 1645 and 885 cm.<sup>-1</sup>. Only one peak was observed on g.l.c. Catalytic reduction of the olefin (900 mg.) gave meso-2,6,10,14-tetramethylpentadecane (900 mg.),  $\alpha_{\rm p}^{25\cdot3}$  0° (Found: C, 85·35; H, 15·15. C<sub>19</sub>H<sub>40</sub> requires C, 85·0; H, 15·0%). I.r. spectroscopy and g.l.c. revealed no impurities.

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