1088. *The Phytadienes and Norphytene, and Their Relation to Some Components of Cigarette Smoke.*

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It is confirmed that acid-catalysed dehydration of phytol gives mixtures of isomeric phytadienes, but it is shown that only one isomer, identical with the neophytadiene of cured tobacco leaf and cigarette-smoke condensate, is obtained on base-catalysed dehydration of phytol. Heating neophytadiene causes some migration of the double bonds but the main product, at 200°, is a mixture of dimers, also present in cigarette-smoke condensate. The synthesis of 3,7,11,15-tetramethylhexadeca-2,4-diene is described. The isolation of norphytene from cigarette smoke is reported.

SEVERAL phytadienes are reported in the literature but most of them are thought really to be mixtures. Dehydration of phytol with acid catalysts has given phytadiene A, considered to be a mixture of isomers (II) and (III),[1,2] and phytadiene C, previously assumed to have structure (III).[2,3] Chromatography of natural phytol on alumina yielded phytadiene B.[2] Neophytadiene (I), isolated from aged flue-cured tobacco leaf, was considered very similar to phytadiene B.[2] Base-catalysed dehydration of phytol yielded a phytadiene having physical properties identical with those of neophytadiene.[4] Geometrical isomerism about the double bonds in the phytadienes means that compound (II) can exist in two forms, and compounds (III) and (IV) in four, apart from optical isomers. We have repeated the preparations of the above phytadienes and examined them by gas chromatography, which revealed the considerable complexity of phytadienes A, B, and C and the simplicity of neophytadiene. Further, the phytadienes were ozonised and the derived acids subjected to gas chromatography. The Table shows the results of these gas chromatograms.

[1] Karrer, Simon, and Zbinden, *Helv. Chim. Acta,* 1944, **27**, 313; Karrer, Kugler, and Simon, *ibid.,* p. 1006.
[2] Rowland, *J. Amer. Chem. Soc.,* 1957, **79**, 5007.
[3] Willstätter, Mayer, and Huni, *Annalen,* 1910, **378**, 73, 109.
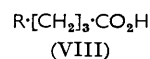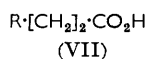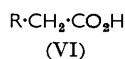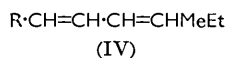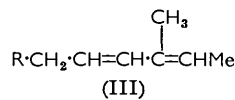[4] Bhati, *Perfumery Essent. Oil Record,* 1963, **54**, 376.

Gas chromatography of phytadienes.

Rel. retention vol. (R_v) of phytadienes (norphytene = 1·00)

A	B	C	Synth. (III)
	1·60(16·9%)		
	1·69(37·0%)	1·69(10·5%)	
1·81(36·0%)	1·83(34·8%)		
			1·85(11%)
2·02(22·1%)		2·02(22·9%)	
2·26(37·8%)		2·24(50·6%)	2·28(6%)
2·44(4·1%)	2·39(11·3%)		
		2·56(11·8%)	2·58(83%)
		2·91(4·2%)	

Wt.-% of acids (V—VIII) obtained on ozonolysis

V	5	52	—
VI	17	38	95
VII	52	10	—
VIII	26	—	—

Neophytadienes *

	X	Y	Z
R_v (%)	1·81(100%)	1·81(100%)	1·82(100%)
Acid (VIII)	100	100	100

* (X) From base-catalysed dehydration of phytol. (Y) From flue-cured tobacco. (Z) From cigarette smoke.

It can be seen that neophytadiene from flue-cured tobacco and cigarette-smoke condensate, and the phytadiene obtained by base-catalysed dehydration of phytol show only one peak each, with the same retention volume in gas chromatograms of the dienes themselves or the acids obtained on ozonolysis. The isolation of only the acid (VIII) from neophytadiene confirms its structure (I). Gas chromatography of the phytadiene obtained by base-catalysed dehydration of phytol[4] revealed another component which we suggested was norphytene (2,6,10,14-tetramethylpentadec-1-ene). We found that the yield of norphytene in this reaction varied between 14% and 49% of the hydrocarbon obtained, and its infrared spectrum showed absorption at 825 cm.$^{-1}$ (trisubstituted double bond), but the band at 890 cm.$^{-1}$ was weaker than in the spectrum of norphytene prepared by another route; the difference probably arose because the double bond in some of the norphytene from the base-catalysed dehydration had moved towards the centre of the chain. A mechanism suggested earlier[5] for the base-catalysed dehydration of αβ-unsaturated alcohols explains the production of the single isomer, neophytadiene.

On gas chromatography, phytadiene A showed three main peaks, one of which had the same retention volume as neophytadiene, and the isolation of the C_{17} acid (VIII) on ozonolysis confirmed its presence. Since considerable amounts of the C_{15} and C_{16} acids (VI and VII) were also obtained the presence of compounds (II) and (III) in phytadiene A is confirmed. Presence of a little of compound (IV) is suggested by isolation of the C_{14} acid (V).

R = Me$_2$CH·[CH$_2$]$_3$·CHMe·[CH$_2$]$_3$·CHMe

$$\begin{matrix} \overset{\displaystyle CH_2}{\underset{\displaystyle \parallel}{}} \\ R\cdot[CH_2]_3\cdot C\cdot CH=CH_2 \\ (I) \end{matrix} \qquad \begin{matrix} \overset{\displaystyle CH_3}{\underset{\displaystyle |}{}} \\ R\cdot[CH_2]_2\cdot CH=C\cdot CH=CH_2 \\ (II) \end{matrix} \qquad \begin{matrix} \overset{\displaystyle CH_3}{\underset{\displaystyle |}{}} \\ R\cdot CH_2\cdot CH=CH\cdot C=CHMe \\ (III) \end{matrix}$$

R·CH=CH·CH=CHMeEt
(IV)

R·CO$_2$H
(V)

R·CH$_2$·CO$_2$H
(VI)

R·[CH$_2$]$_2$·CO$_2$H
(VII)

R·[CH$_2$]$_3$·CO$_2$H
(VIII)
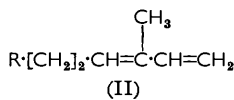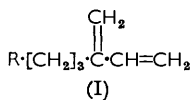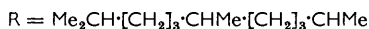
[5] Ohloff, *Annalen,* 1959, **627**, 79.

The phytadiene B, obtained by us on chromatography of a sample of natural phytol, is not necessarily similar in composition to that prepared earlier.[2]   On gas chromatography, our phytadiene B showed two major peaks one of which corresponded to neophytadiene, and two (minor) fractions having retention volumes similar to those given by isomers (III) and (IV).   Further evidence for the small contribution of the last two compounds to the composition of phytadiene B is provided by the weak absorption band at 962 cm.[-1]. Phytadiene B thus probably consists of neophytadiene and one other major constituent.

The gas chromatogram of phytadiene C showed four main peaks, and gave on ozonolysis chiefly the C_{14} and C_{15} acids (V and VI), indicating compounds (III) and (IV) were present. There was no contribution from compound (I) and little from (II).   The infrared spectrum of phytadiene C has a very strong band at 962 cm.[-1], indicating predominance of the *trans*-configuration about the disubstituted double bonds.   As has been suggested,[2] and demonstrated,[6] the strong acid used to obtain phytadiene C from phytol results in the migration of the double bond, but there is no reason for this process to stop at compound (III).   In fact, migration of the double bonds evidently proceeds in the direction (II) $\longrightarrow$ (III) $\longrightarrow$ (IV), whereafter no further shift into the chain would be expected but rather a reversal towards the isomer (II) since a proton usually attacks the less substituted end of a double bond.   To gain more information, phytadiene C was passed through a preparative-scale gas-chromatography column; fractions corresponding to the first and the third peaks listed in the Table were isolated.   The former had a *cis*-orientation about the disubstituted double bond, as shown by an infrared band at 760 cm.[-1] and an ultraviolet absorption maximum at 239 mμ (log ε 4·1); appearance early in the gas chromatogram is consistent with the lower boiling point associated with *cis*-isomers.   The diene in the third fraction gave the strong band at 962 cm.[-1] and had ultraviolet absorption at 236 mμ (log ε 4·37).   However, ozonolysis yielded almost equal amounts of the C_{14} and the C_{15} acid (V and VI), showing the contribution of both compounds (III) and (IV).   The presence of these in phytadiene C minimises the usefulness of this substance as a pure compound for the determination of the absolute configuration of phytol at C-7.[7]

By a Wittig reaction with triphenyl-3,7,11-trimethyldodecylphosphonium bromide and 2-methylbut-2-enal we obtained a good yield of phytadiene.   Gas chromatography showed that there was chiefly one geometrical isomer and this was easily separated from the small amounts of the other two isomers by preparative-scale gas chromatography.   An infrared spectrum showed that mainly the isomer having a *trans*-disubstituted double bond had been obtained.   As 2-methylbut-2-enal also probably exists mainly in the *trans*-form (cf. tiglic and angelic acid), the diene prepared is believed to be *trans,trans*-3,7,11,15-tetra-methylhexadeca-2,4-diene.   The retention volume of this phytadiene corresponded to one of the smaller peaks in the gas chromatogram of phytadiene C, and on ozonolysis it afforded the C_{15} acid (VI).

The acids (V—VIII) were synthesised for comparison with the acids obtained on ozonolysis of the phytadienes.   Heating 3,7,11-trimethyldodecan-1-ol with potassium hydroxide gave an excellent yield of 3,7,11-trimethyldodecanoic acid (VI); treatment of 1-bromo-3,7,11-trimethyldodecane with alcoholic potassium hydroxide gave 3,7,11-tri-methyldodec-1-ene which on ozonolysis afforded 2,6,10-trimethylundecanoic acid (V); hypoiodite oxidation of methyl 4,8,12-trimethyltridecyl ketone gave mainly 5,9,13-tri-methyltetradecanoic acid (VIII), with some 4,8,12-trimethyltridecanoic acid (VII).

It has been reported that when neophytadiene is heated at 180° the diene system migrates towards the centre of the chain.[6]   We have reinvestigated this reaction but find that, although a little such migration occurs, the main product is a mixture of dimers produced by Diels–Alder condensation.[8]   After neophytadiene had been heated at 190—200°, distillation yielded a lower-boiling fraction, shown to be mainly unchanged

[6] Rodgman, *J. Org. Chem.*, 1959, **24**, 1916.
[7] Crabbe, Djerassi, Eisenbraun, and Liu, *Proc. Chem. Soc.*, 1959, 264.
[8] Johnstone and Quan, *J.*, 1963, 935, 2221.

neophytadiene by gas chromatography, and a higher-boiling fraction containing the hydrocarbons (IX—XII). Chromatography of the latter fraction separated the cyclohexenes (IX and X) from the vinyl cyclohexenes (XI and XII). The last two components were not investigated extensively as they formed only a small proportion of the

[R = 4,8,12-trimethyltridecyl]
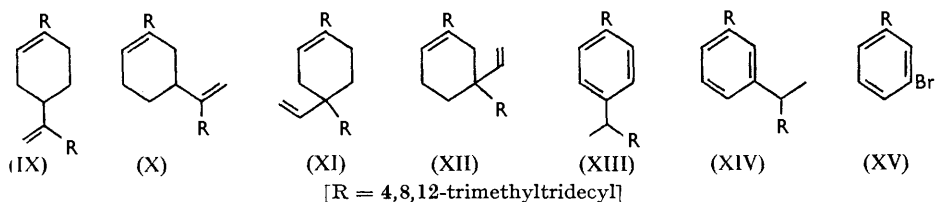
mixture; their proposed structures rest mainly on infrared spectra and analogy with earlier work.[8] The mixture of compounds (IX) and (X) absorbed two equivalents of hydrogen, yielding saturated hydrocarbons, and on dehydrogenation afforded benzenoid hydrocarbons which were separated by chromatography into the *para-* and *meta-*isomers (XIII) and (XIV), the latter being retained more strongly on alumina. Oxidation of these isomers with nitric acid produced, respectively, terephthalic and isophthalic acid. These hydrocarbons (XIII) and (XIV) were then synthesised and their infrared spectra and relative retention volumes on gas chromatography were identical with those of the hydrocarbons obtained by dehydrogenation of the neophytadiene dimers. Treatment of *m*-bromobenzaldehyde with 3,7,11-trimethyldodecylmagnesium bromide and dehydration of the resulting secondary alcohol yielded an olefin which was hydrogenated to *m*-bromo-(4,8,12-trimethyltridecyl)benzene (XV). Poor yields of Grignard reagent were obtained from this product, so the lithium derivative was prepared by exchange with n-butyl-lithium,[9] and this with methyl 4,8,12-trimethyltridecyl ketone gave a tertiary alcohol which on dehydration and then hydrogenation yielded the required compound (XIV). The *para*-isomer (XIII) was obtained similarly from *p*-bromobenzaldehyde. Earlier experiments to reverse the order of addition of the side-chains to the benzenoid nucleus were unsuccessful because of the failure of 2-*m*-bromophenyl-1,3-dioxolan to form an organo-magnesium or -lithium compound, the dioxolan ring being cleaved in each case.

We then re-examined the phytadienes of cigarette-smoke condensate. The first fractions from the column chromatogram that contained diene components (as shown by infrared and ultraviolet spectroscopy) were examined by gas chromatography. There was substantially only one phytadiene, which we showed to be neophytadiene (cf. ref. 6), this being accompanied by <1% of its weight of other phytadiene isomers. Further examination and column chromatography of these first fractions enabled us to isolate norphytene and the neophytadiene dimer mixture (IX—XII) from cigarette-smoke condensate. The norphytene was identical with the synthetic material described earlier. On reduction it gave norphytane, and on ozonolysis methyl 4,8,12-trimethyltridecyl ketone. The presence of norphytene in the condensate is unusual, especially as none was found in the extracts of flue-cured tobacco leaf. It possibly arises by decarboxylation of phytenic acid either present in the leaf or formed by oxidation of phytol during smoking. The dimer mixture was present in small amount and may perhaps have been formed during working-up of the smoke condensate. However, at no time was the condensate subjected to temperatures above 80°, and that only for short periods, so it is likely that the dimers were formed during the smoking process.

EXPERIMENTAL

Unless stated otherwise, the following were used throughout: (i) light petroleum, b. p. 40—60°; (ii) alumina, washed with ethyl acetate; Brockmann's grade I; (iii) silica gel (100—

[9] Gilman, Langham, and Moore, *J. Amer. Chem. Soc.*, 1940, **62**, 2327.

8 X

200 mesh), activated at 110° for 5 hr. Except in one case mentioned below, hydrogenations were performed at atmospheric pressure and temperature with platinic oxide in ethyl acetate.

Gas chromatography. In preparative-scale work, samples (0·5 ml.) were placed on a 5' × 1" column of firebrick (30—60 mesh; Johns-Manville) coated with 20% of Reoplex and operated at 180° with a nitrogen flow of 250 ml./min. The eluate was collected at −70°. In analytical work, the phytadienes and the branched long-chain acids (V—VIII) were chromatographed at 154° and 194°, respectively, on a column (4' × $\frac{3}{16}$") containing 5% of poly(ethylene glycol) adipate on firebrick (80—100 mesh) with a carrier nitrogen flow of 55 ml./min. The benzene compounds (XIII) and (XIV) were chromatographed at 240° on a column (2' × $\frac{1}{8}$") containing 3% of polycyclohexanedimethanol adipate on firebrick (80—100 mesh), with a hydrogen flow of 35 ml./min. The retention volumes relative to squalane (1·00) were 25·0 for the *meta*-isomer (XIV), and 32·8 for the *para*-isomer (XIII).

Methyl 4,8,12-Trimethyltridecyl Ketone.—This was prepared by ozonolysis of phytol.[10]

3,7,11-Trimethyldodecan-1-ol (Hexahydrofarnesol).—Farnesyl acetate was hydrogenated with palladium–calcium carbonate in ethyl acetate.[10] Saponification of the product and chromatography on silica gel gave 3,7,11-trimethyldodecan-1-ol (68%), b. p. 152—154°/15 mm.

1-Bromo-3,7,11-trimethyldodecane.—A mixture of 3,7,11-trimethyldodecan-1-ol (16·9 g.), concentrated sulphuric acid (4 ml.), and 48% aqueous hydrobromic acid (14 ml.) was refluxed for 5 hr.[11] The organic layer was separated, washed with saturated sodium chloride solution, dried (MgSO$_4$), and chromatographed on silica gel (80 g.). Elution with light petroleum gave 1-bromo-3,7,11-trimethyldodecane (14·8 g.), b. p. 140—145°/0·8 mm.

2-m-Bromophenyl-1,3-dioxolan.—A mixture of *m*-bromobenzaldehyde (9·3 g.), ethylene glycol (4·6 g.), benzene (40 ml.), and toluene-*p*-sulphonic acid (15 mg.) was refluxed in a Dean–Stark apparatus for 4 hr. The organic material was washed with sodium hydrogen carbonate solution, dried (MgSO$_4$), and distilled, to give 2-*m*-*bromo*-1,3-*dioxolan*, b. p. 106—107°/1 mm. (Found: C, 47·5; H, 4·4; Br, 35·0. C$_9$H$_9$BrO$_2$ requires C, 47·2; H, 4·0; Br, 34·9%).

m - Bromo - (4,8,12 - trimethyltridec - 1 - enyl)benzene. — 3,7,11 - Trimethyldodecylmagnesium bromide (from 11·0 g. of 1-bromo-3,7,11-trimethyldodecane and 0·91 g. of magnesium in 30 ml. of ether) was treated dropwise with *p*-bromobenzaldehyde (7 g.) in ether (10 ml.), and after 1 hr. the mixture was refluxed for 1 hr., then decomposed with dilute sulphuric acid. The ether layer was washed with sodium hydrogen carbonate solution and dried (MgSO$_4$). Distillation and chromotography of the residue on silica gel (100 g.) gave, on elution with light petroleum, a hydrocarbon.[12] Further elution with ether yielded a mixture (10·9 g.) of unchanged *p*-bromobenzaldehyde and 4-*p*-bromophenyl-4,8,12-trimethyltridecan-1-ol. Most of the aldehyde was distilled off under reduced pressure and the residue heated with anhydrous potassium hydrogen sulphate (0·6 g.) for 2 hr. at 170°/2 mm. Chromatography on silica gel (40 g.) and elution with light petroleum gave a fraction (3·24 g.) which on distillation yielded *p*-*bromo*-(4,8,12-*trimethyltridecyl-1-enyl*)*benzene* (1·91 g.), b. p. 170°/0·4 mm., $\nu_{max.}$ 967 (*trans*-disubstituted double bond), 830br, and 780 cm.$^{-1}$ (Found: C, 69·4; H, 9·3; Br, 21·1. C$_{22}$H$_{35}$Br requires C, 69·6; H, 9·3; Br, 21·1%). Further elution with ether yielded some oxygenated material (3·5 g.) which, from its infrared spectrum, was possibly *p*-(3,7,11-trimethyldodecyl)-benzaldehyde, arising by coupling of the Grignard reagent at the bromine of *p*-bromobenzaldehyde. Hydrogenation of *p*-bromo-(4,8,12-trimethyltridecyl-1-enyl)benzene gave p-*bromo*-(4,8,12-*trimethyltridecyl*)*benzene*, b. p. 176°/0·3 mm., $\nu_{max.}$ 822br and 790 cm.$^{-1}$ (Found: C, 69·6; H, 9·6; Br, 21·2. C$_{22}$H$_{37}$Br requires C, 69·3; H, 9·8; Br, 20·9%).

p-(1,5,9,13 - Tetramethyltetradecyl) - (4,8,12-trimethyltridecyl)benzene.—To the preceding bromide (1·53 g.) in ether (10 ml.) under nitrogen was added n-butyl-lithium (1·1 equiv. of a 1·2N-solution in ether). The mixture was refluxed for 20 min., then cooled. Methyl 4,8,12-tri-methyltridecyl ketone (1·43 g.) in ether (5 ml.) was added slowly, and the whole left overnight and then refluxed for 1 hr. The complex was decomposed with cold, dilute sulphuric acid and the ether layer was washed with water and dried (MgSO$_4$). Distillation of the ether gave a residue which was chromatographed on silica gel (25 g.). Elution with light petroleum yielded some hydrocarbon (0·6 g.), and further elution with ether gave crude 1,5,9,13-tetra-methyl-1-*p*-(4,8,12-trimethyltridecylphenyl)tetradecan-1-ol (1·98 g.) which was heated with

[10] Fischer, *Annalen,* 1928, **464**, 69.
[11] Kamm and Marvel, *Org. Synth.,* Coll. Vol. I, 1st edn., p. 23.
[12] Cf. Karrer and Helfenstein, *Helv. Chim. Acta,* 1931, **14**, 78.

anhydrous potassium hydrogen sulphate (0·1 g.) at 170°/0·3 mm. The product was chromato-graphed on alumina; elution with light petroleum gave an isomer mixture (0·95 g.), b. p. 260°/0·3 mm., $v_{max.}$ 894 and 850—800br cm.$^{-1}$ (Found: C, 87·0; H, 13·2. Calc. for $C_{40}H_{72}$: C, 86·9; H, 13·1%). Hydrogenation of this gave p-(1,5,9,13-*tetramethyltetradecyl*)-(4,8,12-*trimethyltridecyl*)*benzene*, b. p. 260° (air-bath)/0·3 mm., $v_{max.}$ 820v.br cm.$^{-1}$ (Found: C, 86·5; H, 13·4. $C_{40}H_{74}$ requires C, 86·6; H, 13·4%).

Similarly, from *m*-bromobenzaldehyde (6·1 g.) and 3,7,11-trimethyldodecylmagnesium bromide was prepared m-*bromo*-(4,8,12-*trimethyltridec*-1-*enyl*)*benzene* (1·81 g.), b. p. 170°/0·4 mm., $v_{max.}$ 965, 768, and 680 cm.$^{-1}$ (Found: C, 69·6; H, 9·4; Br, 21·2. $C_{22}H_{35}Br$ requires C, 69·6; H, 9·3; Br, 21·1%). Hydrogenation afforded m-*bromo*-(4,8,12-*trimethyltridecyl*)*benzene* (1·6 g.), b. p. 168°/0·3 mm., $v_{max.}$ 772 and 688 cm.$^{-1}$ (Found: C, 69·3; H, 9·6; Br, 21·1. $C_{22}H_{37}Br$ requires C, 69·3; H, 9·8; Br, 20·9%). This bromo-compound after exchange with n-butyl-lithium and treatment with methyl 4,8,12-trimethyltridecyl ketone gave an isomer mixture (0·19 g.), b. p. 270° (air-bath)/0·3 mm., $v_{max.}$ 890, 790, 718, and 700 cm.$^{-1}$ (Found: C, 86·7; H, 13·2. Calc. for $C_{40}H_{72}$: C, 86·9; H, 13·1%). Hydrogenation of this mixture gave m-(1,5,9,13-*tetra-methyltetradecyl*)-(4,8,12-*trimethyltridecyl*)*benzene* (0·18 g.), b. p. 270° (air-bath)/0·3 mm., $v_{max.}$ 787 and 702 cm.$^{-1}$ (Found: C, 86·8; H, 13·2. $C_{40}H_{74}$ requires C, 86·6; H, 13·4%).

Action of Heat on Neophytadiene.—Synthetic neophytadiene (1 g.) was heated under nitrogen at 190—200° for 1 hr. Distillation yielded a phytadiene fraction (0·2 g.), b. p. 130—140° (air-bath)/0·8 mm., and an oil (0·8 g.), b. p. 285° (air-bath)/0·8 mm., $v_{max.}$ 997, 908, and 888 cm.$^{-1}$. Gas chromatography of the phytadiene fraction showed it to be a mixture of isomers, but mainly unchanged neophytadiene. The high-boiling oil (0·115 g.) was chromatographed on alumina (115 × 1 cm.); elution with light petroleum yielded (a) a mixture (0·02 g.), b. p. 208—210° (air-bath)/0·5 mm., $v_{max.}$ 997 and 908 cm.$^{-1}$ (Found: C, 86·2; H, 13·9. Calc. for $C_{40}H_{76}$: C, 86·25; H, 13·75%), and (b) another mixture (0·08 g.), b. p. 226° (air-bath)/0·5 mm., $v_{max.}$ 888 cm.$^{-1}$ (Found: C, 86·5; H, 13·7%). On hydrogenation, fraction (a) and (b) absorbed 2 equiv., of hydrogen to yield the saturated hydrocarbon mixtures (a'), b. p. 212—214° (air-bath)/0·3 mm. (Found: C, 85·6; H, 14·0. Calc for $C_{40}H_{80}$: C, 85·6; H, 14·4%), and (b') b. p. 228° (air-bath)/0·5 mm. (Found: C, 85·6; H, 14·1. Calc. for $C_{40}H_{80}$: C, 85·6; H, 14·4%). Fraction (b) was heated with 10% palladium–charcoal at 240° for 1 hr. under nitrogen. The charcoal was extracted with ether, and the ether distilled off, to yield an oily residue which was chromatographed on alumina (115 × 1 cm., for 65 mg.). Elution with light petroleum gave two narrowly separated fractions: (i) p-(1,5,9,13-*tetramethyltetradecyl*)-(4,8,12-*trimethyl-tetradecyl*)*benzene* (XIII) (28 mg.), b. p. 260° (air-bath)/0·2 mm., $\lambda_{max.}$ 251, 258, 263, 265, and 272 mμ (log ε 2·40, 2·53, 2·63, and 2·64) (Found: C, 86·9; H, 13·7. $C_{40}H_{74}$ requires C, 86·6; H, 13·4%), and (ii) m-(1,5,9,13-*tetramethyltetradecyl*)-(4,8,12-*trimethyltetradecyl*)*benzene* (XIV) (33 mg.), b. p. 280° (air-bath)/0·3 mm., $\lambda_{max.}$ 258, 263, and 271 mμ (log ε 2·42, 2·51, and 2·42) (Found: C, 86·4; H, 13·4%). Fraction (i) (11 mg.), when heated with concentrated nitric acid (1 part) and water (2 parts) at 180—190° for 24 hr., yielded terephthalic acid (2·5 mg.) (infrared spectrum identical with that of an authentic sample). Similarly, fraction (ii) (19 mg.) gave isophthalic acid (4·5 mg.).

Norphytene.—Methylene-tri-*p*-tolylphosphorane (from methyltri-*p*-tolylphosphonium bromide [13] and n-butyl-lithium) was shaken with methyl 4,8,12-trimethyltridecyl ketone [14] (1 equiv.) under nitrogen for 3 hr., then heated in a sealed tube at 70° for 3 hr. Evaporation of the ether and chromatography on alumina gave, on elution with light petroleum, *norphytene* (25%), b. p. 110° (air-bath)/0·3 mm., n_D^{20} 1·4491, $v_{max.}$ 888 cm.$^{-1}$ (Found: C, 85·8; H, 14·2. $C_{19}H_{38}$ requires C, 85·6; H, 14·4%). Hydrogenation gave norphytane, b. p. 108° (air-bath)/0·5 mm. (Found: C, 84·7; H, 14·7. Calc. for $C_{19}H_{40}$: C, 85·0; H, 15·0%).

Triphenyl-3,7,11-trimethyldodecylphosphonium Bromide.—1-Bromo-3,7,11-trimethyldodecane (1 g.), triphenylphosphine (0·9 g.), and nitromethane (10 ml.) were refluxed for 6 hr. The solvent was removed *in vacuo* and addition of dry ether to the residue gave a precipitate which was filtered off, washed with dry ether, and kept in a vacuum-desiccator. The crude triphenyl-3,7,11-trimethyldodecylphosphonium bromide (0·96 g.) was used without further purification.

3,7,11,15-Tetramethylhexadeca-2,4-diene.—Triphenyl-3,7,11-trimethyldodecylphosphonium bromide (0·96 g.), suspended in dry ether (15 ml.), was treated with one equiv. of n-butyl-lithium in ether (1·4 ml. of 1·24N-solution) and shaken under nitrogen for 45 min. The resulting

[13] Wittig, Weigmann, and Schlosser, *Chem. Ber.*, 1961, **94**, 676.
[14] Burrell, Jackman, and Weedon, *Proc. Chem. Soc.*, 1959, 263.

red solution was treated with 2-methylbut-2-enal [15] (0·15 g.) in ether (5 ml.), shaken for 1 hr., and then refluxed for 5 hr. under nitrogen. The ether was decanted and evaporated, to leave a residue which was chromatographed on alumina. Elution with light petroleum yielded 3,7,11,15-*tetramethylhexadeca-2,4-diene* (0·19 g., 40%), b. p. 126°/0·3 mm., $\nu_{max.}$ 962 cm.$^{-1}$, $\lambda_{max.}$ 234 mμ (log ε 4·37) (Found: C, 86·1; H, 13·9. $C_{20}H_{38}$ requires C, 86·2; H, 13·8%).

Phytadiene A.—This was prepared by dehydration of phytol with anhydrous oxalic acid in dioxan [1,2] (Found: C, 86·6; H, 13·4. Calc. for $C_{20}H_{38}$: C, 86·2; H, 13·8%).

Phytadiene B.—Phytol (British Drug Houses Ltd.) (20 g.) was chromatographed on alumina (200 g.). Elution with light petroleum gave a hydrocarbon fraction [2] (190 mg.), and elution with ether gave phytol, b. p. 156—158°/0·7 mm. The hydrocarbon fraction was rechromatographed to separate small amounts of saturated hydrocarbons from the phytadiene B (Found: C, 86·4; H, 13·7. Calc for $C_{20}H_{38}$: C, 86·2; H, 13·8%).

Phytadiene C.—This was prepared by dehydration of phytol with phthalic anhydride and toluene-*p*-sulphonic acid in benzene [2,3] (Found: C, 86·2; H, 13·8. Calc. for $C_{20}H_{38}$: C, 86·2; H, 13·8%).

Synthetic Neophytadiene (3-Methylene-7,11,15-trimethylhexadec-1-ene).—Phytol was heated to 180—190°/15 mm. with twice its weight of powdered potassium hydroxide.[4] The distillate was chromatographed on alumina. Elution with light petroleum yielded norphytene and then neophtyadiene, b. p. 128°/0·5 mm. n_D^{21} 1·4622 (Found: C, 86·3; H, 13·6. Calc. for $C_{20}H_{38}$: C, 86·2; H, 13·8%).

Neophytadiene from Flue-cured Tobacco.—Flue-cured tobacco leaf (2 kg.) was extracted exhaustively with light petroleum. Evaporation of the extract left a residue (6·79 g.) which was treated with a hot saturated solution of urea in methanol (20 ml.). The precipitate formed on cooling was filtered off and washed with light petroleum, and the combined filtrates were diluted with water. The petroleum layer was separated, washed with water, dried (Na_2SO_4), and evaporated, leaving a residue (4·23 g.) which was treated twice more in the same way with urea and methanol. The final residual oil (3·0 g.) was chromatographed on alumina (60 g.). Elution with light petroleum gave some long-chain paraffins [16] and then neophytadiene [2] (0·52 g.), b. p. 115—120°/0·2 mm., n_D^{19} 1·4630.

Phytadienes from Cigarette Smoke.—Infrared and gas-chromatographic examination of fractions P.2—4 (see below) from the chromatography of cigarette-smoke condensate showed the presence of phytadienes, mainly in P.3, and that there was one major constituent, neophytadiene. Fraction P.3 was distilled and a cut (1·0 g.), b. p. 116—122°/0·4 mm., containing the phytadienes and norphytene was collected. Further chromatography on alumina and distillation yielded neophytadiene, b. p. 130°/0·8 mm., n_D^{20} 1·4636.

Ozonolysis of the Phytadienes.—The phytadienes were ozonised in methylene chloride at —70°, care being taken not to pass in an excess of ozone. The ozonides were decomposed by stirring them with a mixture (1 : 1) of 10% aqueous sodium carbonate and hydrogen peroxide (100-vol.).[17] The resulting acids were extracted with 5% aqueous potassium hydroxide and subjected to gas chromatography.

3,7,11-Trimethyldodecanoic Acid.—3,7,11-Trimethyldodecan-1-ol (0·71 g.) was heated with powdered potassium hydroxide (1 g.; fused at red heat for 15 min.) at 260° for 3 hr., whereafter evolution of hydrogen almost ceased.[18] The residue was extracted with water and ether. Acidification of the aqueous layer and extraction with light petroleum gave 3,7,11-*trimethyldodecanoic acid* (0·65 g., 87%), b. p. 142—143°/0·5 mm. (Found: C, 74·7; H, 12·4. $C_{15}H_{30}O_2$ requires C, 74·3; H, 12·5%).

2,6,10-Trimethylundecanoic Acid.—1-Bromo-3,7,11-trimethyldodecane (1·1 g.) was refluxed for 3 hr. with 20% ethanolic potassium hydroxide (10 ml.), then diluted with water and extracted with ether. Evaporation gave a residue which was chromatographed on alumina. Elution with light petroleum yielded 3,7,11-*trimethyldodec-1-ene* (0·2 g.), b. p. 112—113°/20 mm., $\nu_{max.}$ 994 and 913 cm.$^{-1}$ (Found: C, 85·9; H, 13·9. $C_{15}H_{30}$ requires C, 85·6; H, 14·4%). Further elution, with ether, gave 1-*ethoxy-3,7,11-trimethyldodecane* (0·57 g.), b. p. 146°/20 mm., $\nu_{max.}$ 1120 cm.$^{-1}$ (Found: C, 79·6; H, 13·8. $C_{17}H_{34}O$ requires C, 80·2; H, 13·5%). 1-Bromo-3,7,11-trimethyldodecane (0·43 g.), when refluxed with quinoline (5 ml.) for 3 hr., yielded

[15] Green and Hickinbottom, *J.*, 1957, 3262.
[16] Carruthers and Johnstone, *Nature*, 1959, **184**, 1131.
[17] Djerassi and Geller, *J. Amer. Chem. Soc.*, 1959, **81**, 2789.
[18] Hochstein and Brown, *J. Amer. Chem. Soc.*, 1948, **70**, 3484; Grundmann, *Chem. Ber.*, 1948, **81**, 510; Weizmann and Garrard, *J.*, 1920, 334.

similarly 3,7,11-trimethyldodec-1-ene (0·08 g.). Ozonolysis of the latter, as for the phytadienes, yielded 2,6,10-*trimethylundecanoic acid*, b. p. 118°/0·5 mm. (Found: C, 73·8; H, 12·1. $C_{14}H_{28}O_2$ requires C, 73·6; H, 12·4%).

Oxidation of Methyl 4,8,12-Trimethyltridecyl Ketone.—A solution of the ketone (1 g.) in methanol (10 ml.) was stirred and treated simultaneously dropwise with solutions of iodine (4 g.) in methanol (100 ml.) and of potassium hydroxide (4·5 g.) in 16 : 1 methanol–water (100 ml.). The mixture was set aside for 1·5 hr., poured into water, acidified, and extracted with ether. The acid portion (0·32 g.) was extracted in the usual way. Gas chromatography showed that 4,8,12-trimethyltridecanoic and 5,9,13-trimethyltetradecanoic acid had been obtained in the ratio 1 : 4·6. The neutral portion contained mainly unchanged ketone.

Extraction of Cigarette-smoke Condensate.[19]—The smoke condensate from 25,000 British cigarettes containing flue-cured tobacco was extracted with light petroleum (4 × 500 ml.) after prior removal of a volatile fraction M.[20] The petroleum extract (266 g.) was chromatographed on alumina. Elution with light petroleum yielded a number of fractions (100 ml.), P.1—25. The residue on the column was eluted with ether (100 ml. fractions, E.26—28). The fractions P.1—4 contained long-chain paraffins, olefins, and dienes (v_{max} 3150, 1645, 1598, 990, 905, and 890 cm.$^{-1}$) and were examined by gas chromatography.

Fraction P.2 was rechromatographed on alumina (115 × 1 cm.). Elution with light petroleum yielded norphytene and then phytadienes. The norphytene, b. p. 92° (air-bath)/0·2 mm., n_D^{19} 1·4500 (5 μg./cigarette), gave methyl 4,8,12-trimethyltridecyl ketone on ozonolysis, and on hydrogenation it absorbed one equiv. of hydrogen, yielding norphytane. The infrared spectrum of this norphytene was identical with that of an authentic specimen. Gas chromatography showed that the phytadiene fraction consisted chiefly of neophytadiene, with about 1% by weight of some lower-boiling isomers.

Fraction P.1 was rechromatographed on alumina (115 × 1 cm.). Elution with light petroleum gave (i) long-chain paraffins, and (ii) olefinic hydrocarbons (v_{max} 890 cm.$^{-1}$). The two fractions were incompletely separated but distillation of the second gave norphytene and then the neophytadiene dimer mixture (IX—XII) (infrared spectrum identical with that of a synthetic specimen). The yield was 0·8 μg./cigarette. On dehydrogenation it afforded the benzenoid hydrocarbons (XIII) and (XIV).

[19] Johnstone and Plimmer, *Chem. Rev.*, 1959, **59**, 885.
[20] Clemo, *Tetrahedron*, 1958, **3**, 168; Johnstone, Quan, and Carruthers, *Nature*, 1962, **195**, 1267.