Synthesis of Asperenone [all-*trans*(*E*)-8-methyl-13-phenyltrideca-4,6,8,10,12-pentaen-3-one], a Pigment of *Aspergillus* Species of Fungi †

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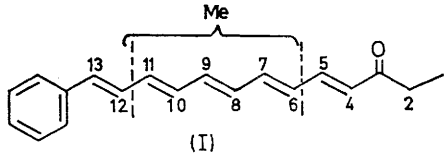
Syntheses of the all-*trans*(*E*)-forms of the 6-methyl (7b), 7-methyl (7a), and 8-methyl (16) isomers of 13-phenyltrideca-4,6,8,10,12-pentaen-3-one are described. Comparison with asperenone, a pigment isolated from *Aspergillus niger* and *A. awamori* establishes structure (16) for the natural product.

ASPERENONE is the name proposed by Jefferson [1] for a yellow pigment isolated from the vegetative mycelium of *Aspergillus niger*. The same pigment was isolated independently by a Japanese group [2] from *Aspergillus awamori* in addition to *A. niger*, and these authors named the pigment asperyellone.‡ Chemical and spectroscopic studies by Jefferson and by the Japanese group have indicated that the pigment is a methyl derivative of 13-phenyltrideca-4,6,8,10,12-pentaen-3-one (1), with the methyl group located somewhere on the side-chain. The exact location of the methyl group could not be determined; Jefferson suggested that it was most likely at C-8 [structure (16)], whereas the Japanese authors favoured C-7 [structure (7a)] or C-6 [structure (7b)]. This paper describes unambiguous syntheses of the all-*trans*(*E*)-forms of the three structures suggested. Comparison with the natural material confirms Jefferson's assignment of structure (16).

The presence of a ketonic group in asperenone was indicated by a positive Brady test and a negative Tollens test, and i.r. data ($\nu_{max.}$ 1670 cm.$^{-1}$) suggested that it was probably an unsaturated ketone. The i.r. spectrum also suggested the presence of a monosubstituted benzene ring ($\nu_{max.}$ 749 and 693 cm.$^{-1}$); this was confirmed by oxidation of the pigment to benzoic acid. The electronic spectrum ($\lambda_{max.}$ 370, 392, and 414 nm.) and hydrogenation evidence (uptake of 5 mol.) indicated a phenyl pentaenone chromophone, and the n.m.r. spectrum showed signals for five aryl protons, nine olefinic protons, and an ethyl group, and a vinyl methyl singlet resonance (τ 8·02). The chemical shift (τ 7·4) of the methylene protons of the ethyl group indicated that they were probably next to the carbonyl group (*i.e.* the compound was an unsaturated ethyl ketone), and hence the pigment was probably a methyl derivative of 13-phenyltrideca-4,6,8,10,12-pentaen-3-one (1).



(I)

† Preliminary communication, G. Pattenden, *Tetrahedron Letters*, 1969, **46**, 4049.

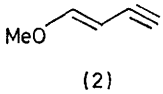
‡ To avoid any confusion the name 'asperenone' is used throughout this paper.

[1] W. E. Jefferson, *Biochemistry*, 1967, **6**, 3479.

[2] J. Yu, G. Tamura, N. Takahashi, and K. Arima, *Agric. and Biol. Chem.* (*Japan*), 1967, **31**, 831.

Spin decoupling studies [2] on the decahydro-derivative of asperenone suggested that the methyl group was not at C-4, C-5, C-12, or C-13, and deuterium exchange studies [1] confirmed that it was probably not at C-4, C-12, or C-13, and, in addition, not at C-2. The group must therefore be at one of the six carbon atoms C-(6—11). The relative abundances of the hydrocarbon fragments in the mass spectra of asperenone and its decahydro-derivative finally led Jefferson to assign structure (16) as the most probable for asperenone, whereas the Japanese authors, on the basis of similar mass spectral analysis, favoured structures (7b) and (7a), and most likely the latter. The stereochemistry of asperenone is assumed to be all-*trans*(*E*), and this assumption was supported by the relative extinction coefficients of the bands associated with the vibrational fine structure of the absorbing molecule in its visible and u.v. spectrum.

Reaction of benzaldehyde with the Grignard reagent derived from 1-methoxybut-1-en-3-yne (2), followed by reduction of the resulting acetylenic alcohol with lithium aluminium hydride, and acid work-up gave aldehyde (3).[3] Condensation of (3) with a *cis–trans* mixture of the phosphonate ester (4) [4] derived from methyl 3-bromo-



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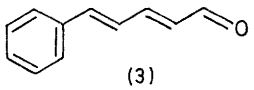

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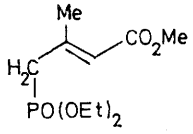

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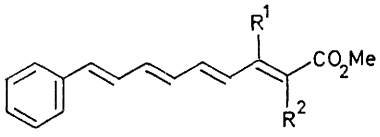

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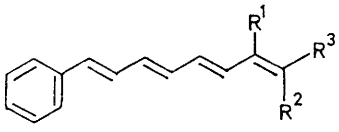

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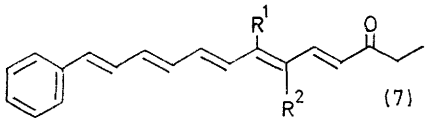
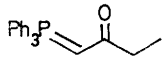


(7)

a; R^1 = Me, R^2 = H b; R^1 = H, R^2 = Me

methylcrotonate, gave a mixture of isomers of tetraene ester, from which the all-*trans*(*E*)-isomer (5a) was separated by chromatography and crystallisation. Published stereochemical data [4] on the use of pure *cis*(*Z*)- and *trans*(*E*)-forms of (4) in aldehyde–phosphonate condensations have established that although almost exclusive *trans*(*E*)-olefination is observed with both isomers, the *cis*(*Z*)-phosphonate loses most of its initial geometry during condensation, whereas the *trans*(*E*)-isomer (4) largely retains its initial geometry. In the condensation between (3) and (4) a 2 : 3 *cis*(*Z*)–*trans*(*E*) mixture of the phosphonate was used. This gave a product whose n.m.r. spectrum indicated that it contained all-*trans*(*E*)-tetraene (5a) contaminated with approximately 15% of the corresponding *cis*(*Z*)-2-isomer; the *cis*-isomer was easily removed in chromatography and crystallisation. Reduction of ester (5a) with lithium aluminium hydride gave the alcohol (6a; $R^3 = CH_2{\cdot}OH$), which was oxidised with manganese dioxide to the corresponding aldehyde (6a; R^3 = CHO). Both the reduction of (5a) and the subsequent oxidation proceeded with no detectable stereochemical changes, and chromatography and crystallisation gave the all-*trans*-(*E*)-aldehyde (6a; R^3 = CHO). A Wittig reaction between (6a; R^3 = CHO) and the phosphorane (8) [5] derived from bromomethyl ethyl ketone, in refluxing di-n-butyl ether, followed by chromatography and crystallisation, then gave the all-*trans*(*E*)-ketone (7a). Earlier attempts to conduct the Wittig condensation in lower-boiling solvents (*e.g.* benzene, tetrahydrofuran, or dioxan) resulted in negligible yields of the polyene ketone (7a). This was largely owing to the correspondingly longer periods required to effect reaction with the stable, unreactive phosphorane (8); both starting aldehyde and ketone product decomposed



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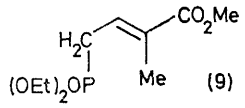


(9)

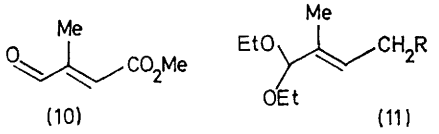
during the prolonged heating. Ketone (7a) had m.p. 150—152° (natural asperenone has m.p. 128—130°) and a mass spectrum closely similar to that of natural asperenone (determined at the same time, and under the same conditions). Both the i.r. spectrum and the τ 2—4 region of the n.m.r. spectrum (see later discussion) of (7a) were however quite different from the data presented for the natural pigment.

By an identical series of transformations, but with the phosphonate ester (9) [4] derived from methyl 4-bromo-2-methylcrotonate in place of (4), the all-*trans*(*E*)-6-methyl ketone (7b) was obtained. The synthetic ketone had m.p. 127—129°, similar to that of natural asperenone, but mixed m.p. depression was observed. The mass spectrum of (7b), similar to that of (7a), was also similar to that of asperenone, but their i.r. spectra and the τ 2—4 region of their n.m.r. spectra (see later discussion) were different and distinguishable.

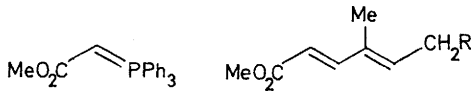
The *trans*(*E*),*trans*(*E*)-triphenylphosphonium salt (13c) was obtained from aldehyde (10) [6] as described previously,[7] after protection of the aldehyde function by

[3] D. Marshall and M. C. Whiting, *J. Chem. Soc.*, 1956, 4082.
[4] G. Pattenden and B. C. L. Weedon, *J. Chem. Soc.* (*C*), 1968, 1984, 1997.
[5] K. Fujiwara, H. Takahashi, and M. Ohta, *Bull. Chem. Soc. Japan*, 1962, **35**, 2042.
[6] K. Sisido, K. Kondô, H. Nozaki, M. Tuda, and Y. Udô, *J. Amer. Chem. Soc.*, 1960, **82**, 2286.
[7] G. Pattenden, J. E. Way, and B. C. L. Weedon, *J. Chem. Soc.* (*C*), 1970, 235.

formation of the diethyl acetal, reduction to (11a), formation of acetate (11b), condensation of the aldehyde of (11b) with phosphorane (12),[8] and treatment of the



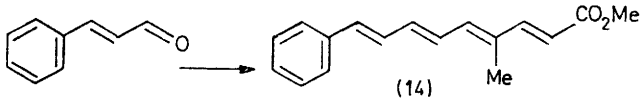
(10) (11)



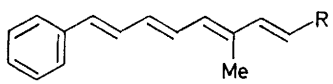
(12) (13)

a; R = OH b; R = OAc c; R = $\overset{+}{P}Ph_3\bar{B}r$

trans(*E*),*trans*(*E*)-diene (13b) thus formed with triphenylphosphonium bromide. Condensation between cinnamaldehyde and the phosphorane derived from salt (13c), led to a mixture of geometrical isomers of ester (14) from which the all-*trans*(*E*)-tetraene was separated by chromatography and crystallisation. The synthesis of



(14)



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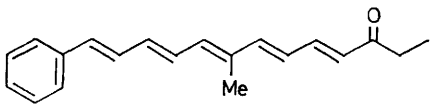
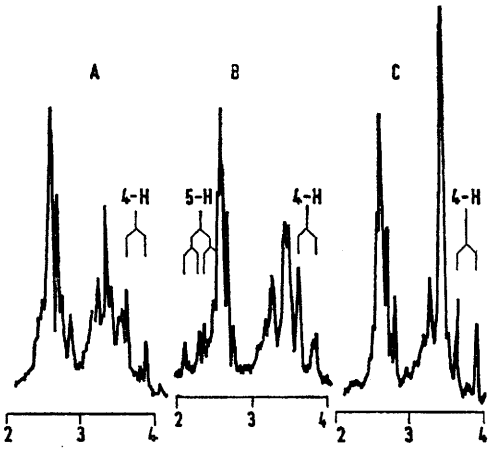


(16)

a; R = CH_2OH b; R = CHO

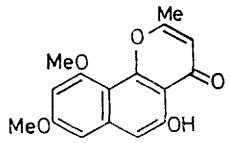
(16) from (14) *via* (15a) and (15b) was then completed in a similar manner to that of the isomeric ketones (7a) and (7b). Chromatography and crystallisation of the final product gave the all-*trans*(*E*)-ketone (16), m.p. and mixed m.p. with natural asperenone 128—130°, with mass spectrum identical with that of the natural product (determined at the same time and under identical conditions). Although insufficient natural asperenone was available for i.r. and n.m.r. spectral comparison under the same conditions, the published spectra of the natural compound were indistinguishable from those obtained for (16).

The synthetic polyene ketones (7a), (7b), and (16) showed closely similar mass spectra and visible light absorption data, and could not be unambiguously distinguished on this basis. In addition, apart from small ($\Delta\tau$ 0·04) chemical shift differences between vinyl methyl resonances, their n.m.r. spectra (τ >6·0) were closely similar. Clear differences were observed in their i.r. spectra, but the three compounds were most readily distinguished by the olefinic proton regions (τ 2·0—4·0) of their n.m.r. spectra (see Figure). Each isomer shows two sets of multiplets, between τ 2·4 and 2·8, [five aryl protons and one olefinic proton in the spectra of (16) and (7b), and five aryl protons in the spectrum of (7a)], and between τ 3·0 and 3·6 (seven olefinic protons). The multiplets between τ 2·4 and 2·8 are of similar complexity

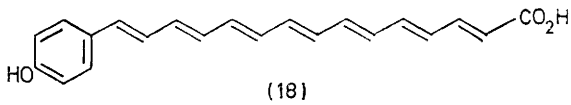


N.m.r. spectra (τ 2—4) of 8-methyl (16) (*A*), 7-methyl (7a) (*B*), and 6-methyl (7b) (*C*) isomers of 13-phenyltrideca-4,6,8,10,12-pentaen-3-one

in each spectrum, but those between τ 3·0 and 3·6 show marked differences. All three spectra show doublets (J 15·5 Hz) centred at τ 3·78 which are assigned to protons at C-4 (α to carbonyl) attached to the *trans*(*E*)-disubstituted 4,5-double bond. In the spectrum of isomer (7a), one of the olefinic protons is chemically shifted from the remainder, and resonates as a double doublet (J 15·5 and 11·5 Hz) centred at τ 2·35. This resonance is assigned to the proton at C-5 (β to carbonyl), which is coupled to the protons at C-4 (J 15·5 Hz) and at C-6 (J 11·5), and deshielded by the *cis* (to it) carbonyl group. A similar double doublet does not appear in the spectrum of natural asperenone. Isomers (7b) and (16) show subtle multiplicity differences, particularly in the τ 3·0—3·6 region. The olefinic proton region of (16) was identical with that published for natural asperenone; that of (7b) was not.



(17)



(18)

The only other pigment isolated from *Aspergillus niger* whose structure is known with certainty is flavasperone;

[8] O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, 1957, **40**, 1242.

this has the chromone structure (17).[9] Amongst fungal pigments, asperenone most closely resembles cortisalin [10] (18), a red pigment isolated [11] from *Corticium salicinum* Fries.

EXPERIMENTAL

M.p.s are corrected, and were determined for samples in evacuated capillaries unless indicated otherwise. As far as possible all operations were carried out under nitrogen. Solutions were dried over magnesium sulphate, and evaporated under reduced pressure. Alumina for chromatography was neutral and Grade III unless stated otherwise. Solvents for chromatography and crystallisation were redistilled before use. Light petroleum refers to fraction b.p. 60—80°.

Except where indicated to the contrary, n.m.r. spectra were determined with a Perkin-Elmer 60 MHz instrument for dilute solutions in deuteriochloroform with tetramethylsilane as an internal standard. Bands were sharp singlets unless otherwise indicated; coupling constants are in Hz.

Visible and u.v. absorption maxima marked by an asterisk were inflections; $\varepsilon \times 10^{-3}$ values are given in parentheses. Molecular weights were determined from mass spectra, measured with an A.E.I. MS9 double-focusing spectrometer.

Where the geometry about a double bond is not specified, it should be assumed to be *trans*(*E*).

5-Phenylpenta-2,4-dien-1-al (3).—Condensation of benzaldehyde with the Grignard reagent prepared from 1-methoxybut-1-en-3-yne, and lithium aluminium hydride reduction of the resulting acetylenic alcohol, followed by acid work-up, according to the method of Marshall and Whiting,[3] gave (78%) the aldehyde, b.p. 116—120°/0·2 mm., which crystallised, and had m.p. 41—43° [lit.,[3] m.p. 42—43°; the b.p. (102—104°) reported by Marshall and Whiting appears to be in error], $\lambda_{max.}$ (95% EtOH) 323 nm., $\nu_{max.}$ (film) 2815, 2740, 1675, 1620, 1590, 1012, 986, 750, and 690 cm.$^{-1}$ τ 0·42 (d, *J* 7·5, CHO), 2·4—3·2 (8H, m, 5 × aryl H and 3 × :CH·), and 3·82 (dd, *J* 15 and 7·5, :C*H*·CHO).

Methyl 3-Methyl-9-phenylnonatetra-2,4,6,8-enoate (5a).—A mixture of *cis*(*Z*)-, and *trans*(*E*)-diethyl 3-methoxycarbonyl-2-methylprop-2-enylphosphonate was prepared as described previously;[4] the n.m.r. spectrum showed the *cis*(*Z*)–*trans*(*E*) ratio to be *ca.* 2 : 3. A solution of sodium methoxide [from sodium (2·3 g.)] in methanol (25 ml.) was added, during 45 min., to a stirred solution of the phosphonate (25 g.) and 5-phenylpenta-2,4-dien-1-al (16 g.) in dimethylformamide (100 ml.) at 30—35°. The mixture was stirred at 20° for 2 hr., then diluted with water, neutralised with glacial acetic acid, and extracted with ether. The extracts were washed with sodium hydrogen carbonate solution and water, dried, and then evaporated. Chromatography of the residue on alumina (Grade I), with benzene as developer, and diethyl ether as eluant, followed by crystallisation from light petroleum gave the *ester* (3·1 g.), m.p. 100—101°, $\lambda_{max.}$ (95% EtOH) 272 (15·6), 345* (52·8), 361·5 (65·3), 377 (57·6) nm., $\nu_{max.}$ ($CHCl_3$) 1705, 1615, 1600, 1585, and 1000 cm.$^{-1}$, τ 2·4—2·8 (m, 5 × aryl H), 3·0—3·6 (m, 6 × :CH), 4·18 (:C*H*·CO_2Me), 6·28 (OMe), and 7·67 (:CMe). The vinyl methyl region of the n.m.r. spectrum of the crude ester product, prior to crystallisation, indicated that the *trans*(*E*)-2-isomer (τ 7·67) was contaminated with the corresponding *cis*(*Z*)-2-isomer (τ 8·05) (*ca.* 15%); the *cis*-isomer was completely removed on crystallisation. (Found: C, 80·1; H, 7·1%; *M*, 254. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%; *M*, 254).

Methyl 2-Methyl-9-phenylnonatetra-2,4,6,8-enoate (5b).—A solution of sodium methoxide [from sodium (2·3 g.)] in methanol (40 ml.) was added, during 1 hr., to a stirred solution of diethyl 3-methoxycarbonyl-3-methylprop-2-enylphosphonate (25 g.) [4] and 5-phenylpenta-2,4-dien-1-al (16 g.) in dimethylformamide (100 ml.) at 35—40°. The mixture was stirred at 20° for 2 hr., and was then worked up as described for the 3-methyl ester. Chromatography as before, and crystallisation from light petroleum gave the *ester* (6·5 g.), m.p. 107—108°, $\lambda_{max.}$ (95% EtOH) 273 (16·0), 347* (51·7), 365 (66·9), and 381 (57·0) nm., $\nu_{max.}$ ($CHCl_3$) 1700, 1625, 1600, 1585, and 1000 cm.$^{-1}$, τ 2·4—2·8 (m, 5 × aryl H and ·C*H*:CMe), 3·0—3·6 (m, 6 × :CH·), 6·22 (OMe), and 8·0 (d, *J* 1·5; :CMe) (Found: C, 80·0; H, 6·9%; *M*, 254. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%; *M*, 254).

Methyl 4-Methyl-9-phenylnonatetra-2,4,6-8-enoate (14).—A solution of 1-acetoxy-5-methoxycarbonyl-3-methylpenta-*trans*(*E*)-2,*trans*(*E*)-4-diene (1 g.) [7] and triphenylphosphonium bromide (1·9 g.) in methanol (20 ml.) was stirred at 20° for 7 days. The methanol was removed under reduced pressure and the oily residue was washed several times with dry ether. Solvents were removed under high vacuum to leave the triphenylphosphonium salt which was used without further purification.

A solution of sodium methoxide [from sodium (0·05 g.)] in methanol (2 ml.) was added during 0·25 hr. to a stirred solution of the phosphonium salt and cinnamaldehyde (0·6 g.) in dimethylformamide (5 ml.) at 20°. The mixture was stirred for 1 hr. at 20° and was then evaporated to dryness *in vacuo*. The residue was dissolved in ether, and the solution was washed with water, dried, and evaporated. Chromatography of the residue in benzene–light petroleum (1 : 1) on alumina followed by crystallisation from light petroleum gave the *all*-trans-*ester* (260 mg.), m.p. 105—107°, $\lambda_{max.}$ (95% EtOH) 272·5 (10·2), 347·5* (48·1), 367 (64·1), and 382 (55·9) nm., $\nu_{max.}$ ($CHCl_3$) 1700, 1615, 1590, 1575, and 995 cm.$^{-1}$, τ 2·4—2·75 (m, 5 × aryl H and ·C*H*:CMe), 3·0—3·6 (m, 5 × :C*H*·), 4·05 (d, *J* 15·5, :C*H*·CO_2Me), 6·21 (OMe), and 8·05 (:CMe) (Found: C, 80·05; H, 6·8%; *M*, 254. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%; *M*, 254).

3-Methyl-9-phenylnonatetra-2,4,6,8-en-1-ol (6a; R^3 = CH_2·OH).—Lithium aluminium hydride (1 g.) in ether (250 ml. was added to a stirred solution of methyl 3-methyl-9-phenylnonatetra-2,4,6,8-enoate (2·5 g.) in ether (500 ml.) at −30° during 1 hr. The mixture was stirred at −30 to −10° for 1 hr., and then water was cautiously added. The mixture was treated with saturated ammonium chloride solution and then extracted with ether. The extracts were washed (H_2O), dried, and evaporated. Crystallisation from benzene–light petroleum gave the *alcohol* (1·7 g., 75%), m.p. 123—124°, $\lambda_{max.}$ (95% EtOH) 312*, 328, 342, and 362 nm., $\nu_{max.}$ ($CHCl_3$) 3400, 1600, 1590, 1070, and 995 cm.$^{-1}$, τ 2·5—3·0 (5 × aryl H), 3·1—3·8 (m, 6 × :CH), 4·3 (t, *J* 7, :C*H*·CH_2), 5·71 (d, *J* 7, CH_2·OH), 8·18 (:CMe), and *ca.* 8·3 (OH) (Found: *M*, 226. $C_{16}H_{18}O$ requires *M*, 226) (Found: C, 81·4; H, 7·9. $C_{16}H_{18}O$,0·5-H_2O requires C, 81·7; H, 8·0%).

[9] B. W. Bycroft, T. A. Dobson, and J. C. Roberts, *J. Chem. Soc.*, 1962, 40.

[10] D. Marshall and M. C. Whiting, *J. Chem. Soc.*, 1957, 537.

[11] J. Gripenberg, *Acta Chem. Scand.*, 1952, **6**, 580.

2-*Methyl*-9-*phenylnonatetra*-2,4,6,8-*en*-1-*ol* (6b; R^3 = CH_2·OH).—Reduction of methyl 2-methyl-9-phenylnonatetra-2,4,6,8-eneoate (6 g.) in ether (1 l.) with lithium aluminium hydride (2·5 g.) in ether (500 ml.) at −30°, as described for the 3-methyl isomer, gave the *alcohol* (3·6 g., 68%), m.p. 120—121° (from benzene–light petroleum), $\lambda_{max.}$ (95% EtOH), 250·5, 259, 316*, 329·5, 345·5, and 366 nm., $\nu_{max.}$ ($CHCl_3$) 3400, 1600, 1585, 1065, and 996 cm.$^{-1}$, $\nu_{max.}$ (Nujol) 3300, 1595, 1580, 1070, 998, 745, and 690 cm.$^{-1}$, τ 2·4—2·9 (m, 5 × aryl H), 3·1—3·9 (7H, m), 5·92 (d, *J* 6, CH_2·OH; collapses to singlet resonance after treatment with D_2O), 8·16 (:CMe), 8·25 (t, *J* 6, OH, exchangeable (Found: *M*, 226. $C_{16}H_{18}O$ requires *M*, 226) (Found: C, 81·3; H, 7·7. $C_{16}H_{18}O,0{\cdot}5H_2O$ requires C, 81·7; H, 8·0%).

4-*Methyl*-9-*phenylnonatetra*-2,4,6,8-*en*-1-*ol* (15a).—Reduction of methyl 4-methyl-9-phenylnonatetra-2,4,6,8-enoate (500 mg.) in ether (100 ml.) with lithium aluminium hydride (0·22 g.) in ether (40 ml.) at −30°, as described for the 3-methyl isomer, and recrystallisation from benzene–light petroleum gave the *alcohol* (380 mg.), m.p. 117—119°, $\lambda_{max.}$ (95% EtOH) 250, 259, 317*, 330, 346, and 366 nm., $\nu_{max.}$ 3390, 1605, 1585, 1080, and 980 cm.$^{-1}$, τ 2·4—2·9 (m, 5 × aryl H), 3·1—4·2 (7H, m), 5·74 (d, *J* 5·5, ·CH_2·OH), *ca.* 7·95br (OH), and 8·08 (:CMe) (Found: *M*, 226. $C_{16}H_{18}O$ requires *M*, 226).

3-*Methyl*-9-*phenylnonatetra*-2,4,6,8-*en*-1-*al* (6a; R^3 = CHO).—A solution of 3-methyl-9-phenylnonatetra-2,4,6,8-en-1-ol (2 g.) in methylene chloride (750 ml.) was shaken with manganese dioxide (50 g.) at 25° for 24 hr. The manganese dioxide was filtered off and washed with methylene chloride. Evaporation of the methylene chloride and chromatography of the residue in benzene–light petroleum (4 : 1) on alumina, followed by concentration and crystallisation from light petroleum, gave the *aldehyde* (0·59 g.), m.p. 126—127°, $\lambda_{max.}$ ($CHCl_3$) 281 (6·6) and 386 (60·6) nm., $\nu_{max.}$ (Nujol) 2710, 1645, 1590, 1570, 995, 746, and 688 cm.$^{-1}$, $\nu_{max.}$ ($CHCl_3$) 2840, 2735, 2720, 1650, 1640, 1595, 1580, 1570, and 995 cm.$^{-1}$, τ −0·14 (d, *J* 7·5, CHO), 2·4—2·8 (m, 5 × aryl H), 3·0—3·8 (6H, m), 4·0 (d, *J* 7·5, :C*H*·CHO), and 7·7 (:CMe) (Found: C, 85·8; H, 7·5%; *M*, 224. $C_{16}H_{16}O$ requires C, 85·7; H, 7·2%; *M*, 224).

2-*Methyl*-9-*phenylnonatetra*-2,4,6,8-*en*-1-*al* (6b; R^3 = CHO).—Oxidation of 2-methyl-9-phenylnonatetra-2,4,6,8-en-1-ol (3 g.) with manganese dioxide (80 g.) in methylene chloride (1200 ml.) (40 hr. at 25°), and isolation as described for the 3-methyl isomer, gave the *aldehyde* (1·05 g.) m.p. 135—136°, $\lambda_{max.}$ ($CHCl_3$) 282 (6·3), 382 (65·2), and 398 (61·0) nm., $\nu_{max.}$ ($CHCl_3$) 2840, 2720, 1655, 1640, 1595, 1580, 1570, and 995 cm.$^{-1}$, τ 0·5 (CHO), 2·4—2·8 (m, 5 × aryl H), 2·9—3·7 (7H, m), and 8·13 (:CMe) (Found: C, 85·6; H, 7·4%; *M*, 224. $C_{16}H_{16}O$ requires C, 85·7; H, 7·2%; *M*, 224).

4-*Methyl*-9-*phenylnonatetra*-2,4,6,8-*en*-1-*al* (15b).—Oxidation of 4-methyl-9-phenylnonatetra-2,4,6,8-en-1-ol (460 mg.) with manganese dioxide (12 g.) in methylene chloride (200 ml.) (24 hr. at 25°), and isolation as described for the 3-methyl isomer gave the *aldehyde* (82 mg.), m.p. 119—123°, $\lambda_{max.}$ (95% EtOH) 280 (5·5) and 384 (59·1) nm., $\nu_{max.}$ ($CHCl_3$) 2800, 2720, 1670, 1600, 1575, and 980 cm.$^{-1}$, τ 0·35 (d, *J* 7·5, CHO), 2·4—2·9 (m, 5 aryl H and ·C*H*:CH·CHO), 3·0—3·5 (5H, m), 3·78 (dd, *J* 7·5 and 15·5, :C*H*·CHO), and 8·04 (:CMe) (Found: C, 85·2; H, 7·4%; *M*, 224. $C_{16}H_{16}O$ requires C, 85·7; H, 7·2%; *M*, 224).

2-*Oxobutylidenetriphenylphosphorane* (8).—Bromination of methyl ethyl ketone (120 g.), with bromine in the presence of potassium chlorate, according to the method of Catch and his co-workers,[12] gave a mixture of 1-bromoethyl methyl ketone (82 g.), b.p. 87—90°/140 mm., (lit.,[12] 86·5—88°/150 mm.), τ (neat) 5·4 (q, *J* 6·5, MeC*H*), 7·66 (Ac), and 8·3 (d, *J* 6·5, CH_3·CHBr), and bromomethyl ethyl ketone (23 g.), b.p. 104—106°/140 mm., n_D^{15} 1·4692 (lit.,[12] 1·4670), τ (neat) 5·88 (CH_2Br), 7·28 (q, *J* 7, CH_2·Me), and 8·93 (t, *J* 7, CH_2·CH_3).

A mixture of bromomethyl ethyl ketone (4 g.) and triphenylphosphine (7 g.) in benzene (25 ml.) was kept at 25° for 1 hr., then at 80° for 1 hr. The triphenylphosphonium salt (9·5 g.) which separated was filtered off, washed with dry ether, dried, and then dissolved in water (600 ml.) and treated with sodium hydroxide (1·5 g.) in water (30 ml.). The phosphorane (7·2 g., 85%) which precipitated was filtered off, then washed with water and crystallised from methylene chloride–ethyl acetate; m.p. 218—220° (lit.,[5] 221—222°), $\nu_{max.}$ (Nujol) 1540 cm.$^{-1}$, τ 2·1—2·6 (15H, m), 5·9br (C*H*:PPh_3), 7·66 (q, *J* 7, CH_2Me), and 8·87 (t, *J* 7, CH_2·CH_3). The same material was obtained from a mixture (4 : 1) of primary and secondary bromides formed by bromination of methyl ethyl ketone; the primary bromide preferentially quaternises the phosphine.

7-*Methyl*-13-*phenyltrideca*-4,6,8,10,12-*pentaen*-3-*one* (7a).—A solution of 3-methyl-9-phenylnonatetra-2,4,6,8-en-1-al (0·2 g.) and 2-oxobutylidenetriphenylphosphorane (1·0 g.) in di-n-butyl ether (40 ml.) was boiled under reflux for 4 hr., and then evaporated to dryness. Chromatography of the residue in benzene–light petroleum (3 : 2) on alumina and crystallisation from benzene–light petroleum gave the *ketone* (64 mg.) as yellow needle clusters, m.p. 150—152°, $\lambda_{max.}$ (light petroleum) 285 (8·0), 295 (8·8), 372 (73·0), 390 (98·0), and 412 (80·2) nm., $\lambda_{max.}$ ($CHCl_3$) 386*, 404, and 420* nm., $\lambda_{max.}$ (EtOH) 404 nm., $\nu_{max.}$ ($CHCl_3$) 1660, 1610, 1593, 1573, 1555, and 998 cm.$^{-1}$, $\nu_{max.}$ (KBr) 1658, 1608, 1594, 1572, 1560, 1005, 980, 932, 900, 886, 754, and 695 cm.$^{-1}$, τ 2·35 (dd, *J* 11·5 and 15·5, 5-H), 2·4—2·8 (*ca.* 5H, m), 3·0—3·6 (*ca.* 7H, m), 3·79 (d, *J* 15·5, 4-H), 7·4 (q, *J* 7·5, CH_2Me), 7·98 (:CMe), and 8·87 (t, *J* 7·5, CH_2·CH_3) (Found: C, 85·9; H, 8·15%; *M*, 278. $C_{20}H_{22}O$ requires C, 86·3; H, 8·0%; *M*, 278).

6-*Methyl*-13-*phenyltrideca*-4,6,8,10,12-*pentaen*-3-*one* (7b).—A solution of 2-methyl-9-phenylnonatetra-2,4,6,8-en-1-al (0·22 g.) and 2-oxobutylidenetriphenylphosphorane (1·0 g.) in di-n-butyl ether (35 ml.) was boiled under reflux for 7 hr., and then evaporated to dryness. Chromatography of the residue in benzene–light petroleum (3 : 2) on alumina and crystallisation from benzene–light petroleum gave the *ketone* (81 mg.) as golden yellow needles, m.p. 130—131° [m.p. 127—129° (Kofler block); depressed to 110—114° on admixture with natural asperenone, m.p. 128—130°], $\lambda_{max.}$ (light petroleum) 371 (74·2), 391·5 (105·0), and 414·5 (92·7) nm., $\nu_{max.}$ ($CHCl_3$) 1655, 1592, 1572, 1555, and 998 cm.$^{-1}$, $\nu_{max.}$ (Nujol) 1680, 1603, 1590, 1572, 1555, 995, 975, 842, 747, and 690 cm.$^{-1}$, τ 2·35—2·8 (*ca.* 6H, m), 3·0—3·6 (*ca.* 7H, m), 3·78 (d, *J* 15·5, 4-H), 7·38 (q, *J* 7·5, CH_3Me), 8·07 (:CMe), and 8·87 (t, *J* 7·5, CH_2·CH_3) (Found: C, 86·05; H, 7·9%; *M*, 278. $C_{20}H_{22}O$ requires C, 86·3; H, 8·0%; *M*, 278).

8-*Methyl*-13-*phenyltrideca*-4,6,8,10,12-*pentaen*-3-*one* (16). A solution of 4-methyl-9-phenylnonatetra-2,4,6,8-en-1-al (75 mg.) and 2-oxobutylidenetriphenylphosphorane (330 mg.) in di-n-butyl ether (25 ml.) was boiled under reflux for 4·5 hr., then evaporated to dryness. Chromatography

[12] J. R. Catch, D. F. Elliott, D. H. Hey, and E. R. H. Jones, *J. Chem. Soc.*, 1948, 274.

of the residue in benzene–light petroleum (3 : 2) on alumina and crystallisation from light petroleum gave the *ketone* (17 mg.) as yellow-orange needles, m.p. 130—132° [m.p. 128—130° (Kofler block); not depressed on admixture with natural asperenone, m.p. 128—130°, $\lambda_{max.}$] (light petroleum) 371·5 (70·5), 392 (94·8), and 415 (81·0) nm., $\nu_{max.}$ (KBr) 1673, 1590, 1574, 1560, 1550, 1224, 1143, 1035, 1005, 990, 983, 880, 868, 848, 833, 752, and 698 cm.$^{-1}$, τ 2·4—2·8 (*ca.* 6H, m), 3·0—3·6 (*ca.* 7H, m), 3·78 (d, *J* 15·5 4-H), 7·4 (q, *J* 7·5, CH_2Me), 8·02 (:CMe), and 8·87 (t, *J* 7·5, CH_2·CH_3) (Found: C, 86·2; H, 7·7%; *M*, 278. $C_{20}H_{22}O$ requires C, 86·3; H, 8·0%; *M*, 278).

I thank Dr. W. E. Jefferson, jun., for a sample of natural asperenone. I also thank Mr. B. W. Maule for running the n.m.r. spectra, and Professor L. Crombie for his interest.

[9/2114 *Received, December 10th,* 1969]