Synthesis of (*Z,E*)- and (*Z,Z*)-α-Farnesenes and -Homofarnesenes

E. David Morgan* and Lorna D. Thompson,
Department of Chemistry, University of Keele, Staffordshire ST5 5BG

The ant substance (*Z,E*)-α-farnesene and its isomer (*Z,Z*)-α-farnesene have been synthesized in an overall yield of 34% in six stages from methyl cyclopropyl ketone and 6-methylhept-5-en-2-one *via* a Wittig condensation. A mixture of the corresponding (*Z,E*)-α-homofarnesene of ants and its (*Z,Z*) isomer were prepared in much poorer yield by the same method and incompletely characterized. The isomeric identification of both insect materials were confirmed.

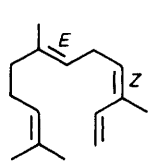
In recent years a number of isomeric farnesenes have been isolated from plant and insect sources, and farnesene homologues or compounds derived from them have been isolated from insects. The identification of α-farnesene isomers from plants has been summarized elsewhere.[1] The first isolation of an α-farnesene from an insect was in 1967, when it was identified as the sole constituent of the Dufour gland of the ant *Aphenogaster longiceps*,[2] and said to be identical with that from Granny Smith apples,[3] which in turn was later identified as chiefly (*E,E*)-α-farnesene.[4] Shortly after, Bergstrom and Löfqvist identified a different α-farnesene in the Dufour glands of three formicine ants.[5] We identified a farnesene isomer and two compounds we called homofarnesene ($C_{16}H_{26}$), and bishomofarnesene ($C_{17}H_{28}$) among the hydrocarbons in the Dufour gland of the ant *Myrmica rubra*.[6] Later we identified these three compounds, plus a fourth, trishomofarnesene ($C_{18}H_{30}$) in the Dufour gland of *Myrmica scabrinodis*.[7] They are present in amounts up to approximately 0.5 μg per insect in the glands of eight *Myrmica* species so far investigated.[8–10]

Too little of these materials was available for conventional structure determination. Initially the farnesene from *Myrmica* ants was identified as (*Z,E*)-α-farnesene, *i.e.* (*Z,E*)-3,7,11-trimethyldodeca-1,3,6,10-tetraene (**1**) by comparison of the relative intensities of a few minor ions in the mass spectrum[6] with values given by Anet,[4] for the four isomers of α-farnesene and two isomers of β-farnesene produced by acid dehydration of nerolidol. Since mass spectral intensities can vary considerably with instrument and conditions, the identification was supported by comparing the retention time of the natural compound on g.l.c. with those of the mixture of farnesenes produced by nerolidol dehydration,[7] using the order of elution given by Anet.[4]

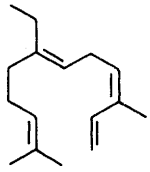
The higher homologues were not available from any source other than the ants. From their mass spectra, they were assigned the structures (**2**), (**3**), and (**4**) respectively, and these structures have recently been confirmed by micro-degradation methods,[11] though the geometry of the double bonds at C-11 in bishomofarnesene (**3**) and at C-3 and C-11 in trishomofarnesene (**4**) remain uncertain. These substances form part of the home-range marking pheromones of these ants.[12]

More recently, isomeric farnesenes and a homofarnesene of different structure have been isolated from *Solenopsis* species,[13] and claimed to have pheromonal properties, with the claim disputed.[14,15] The subject has been reviewed.[16]

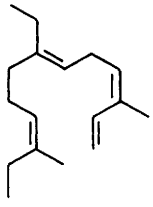
We wished to find a method of synthesis that could be applied to (*Z,E*)-α-farnesene and its higher homologues, if possible, stereospecifically, to confirm our structural assignments, to settle the remaining ambiguities of geometry, and to provide sufficient synthetic material for behavioural experiments. We describe here a stereoselective method which enabled us to prepare (*Z,E*)-α-farnesene and (*Z,Z*)-α-farnesene in good yield and (*Z,E*)-α-homofarnesene and (*Z,Z*)-α-homofarnesene in poor yield.



(**1**)



(**2**)



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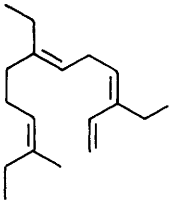
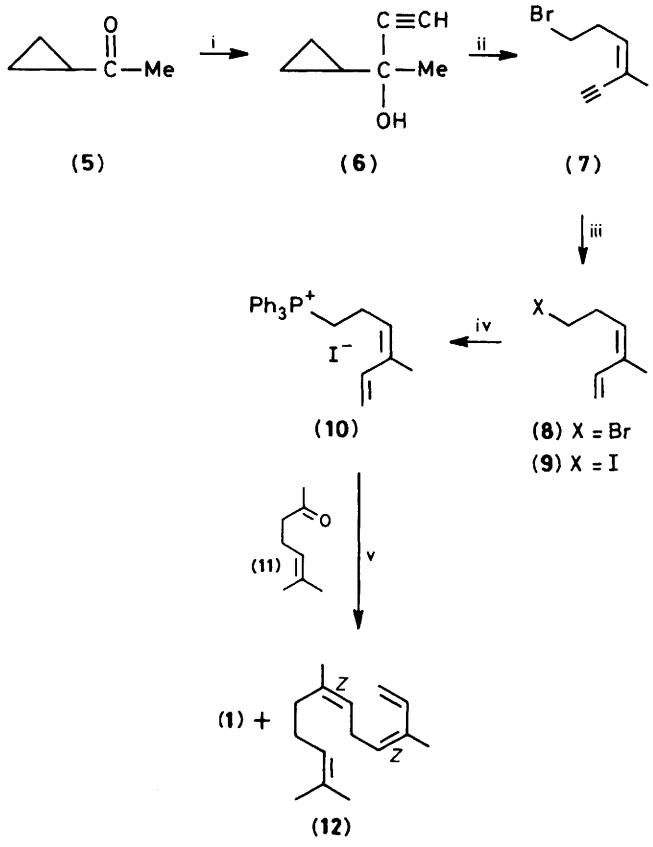


(**4**)

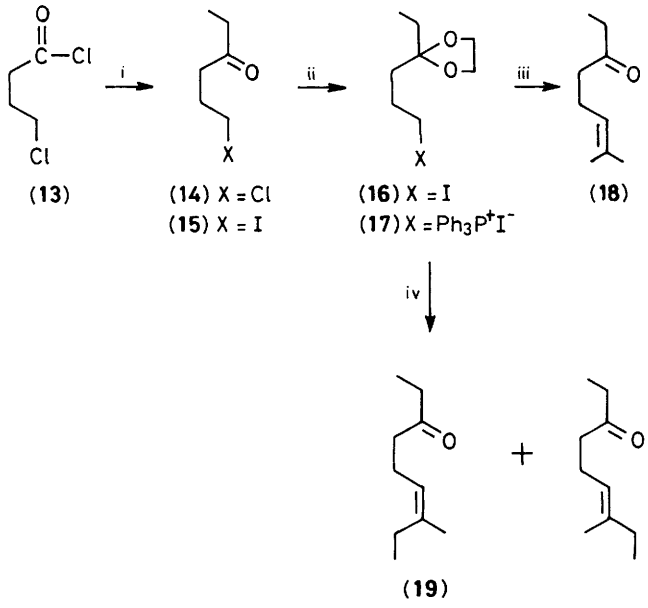
Results and Discussion

The essential steps for a general synthesis of the series were to form the trisubstituted (*Z*)-3 double bond and the (*E*)-6 double bond, the 1,3-conjugated diene and to produce methyl or ethyl branches at C-3, C-7, and C-11 as required. The C-1 to C-6 fragment for compounds (**1**), (**2**), and (**3**) was prepared (as outlined in Scheme 1) by sodium acetylide addition[17] to methyl cyclopropyl ketone (**5**), to give the carbinol (**6**) which rearranged in hydrobromic acid to give the (*Z*)-bromide (**7**), free of contamination by the (*E*) isomer,[18] as determined by ^{13}C and ^{1}H n.m.r. spectra. The triple bond of the bromide (**7**) hydrogenated very slowly to give the bromodiene (**8**) with the (*Z*)-3 configuration intact. When the carbinol produced from reaction of methyl cyclopropyl ketone (**5**) and vinyl-lithium was rearranged,[19] a mixture of (*Z*)- and (*E*)-dienes was formed, in which the (*E*) isomer predominated. The bromide salt resulting from refluxing the bromodiene (**8**) with triphenylphosphine could not be induced to crystallize so the bromide (**8**) was converted into the corresponding iodide (**9**) which gave a more readily crystalline triphenylphosphonium salt (**10**). A similar set of reactions was planned, using ethyl cyclopropyl ketone for the synthesis of trishomofarnesene.

Carbon atoms 7 to 12 of the farnesene structure are available in the form of 6-methylhept-5-en-2-one (**11**). To complete the stereospecific synthesis, it would be necessary to produce a *trans* double bond in the Wittig reaction between the phosphonium salt (**10**) and the ketone (**11**). The method of Schlosser and Christmann for *trans*-selective alkene synthesis[20,21] gave a mixture of (*Z,Z*)- and (*Z,E*)-α-farnesenes in 33% yield with the (*Z,Z*) isomer predominating. A comparable ratio of (*Z,Z*)- to (*Z,E*)-α-farnesene was obtained, after careful exploration of



Scheme 1. i, C_2H_2, Na, NH_2; ii, HBr; iii, H_2–Pd; NaI; iv, Ph_3P; v, BuLi, DME



Scheme 2. i, EtMgBr, $FeCl_3$; NaI; ii, $(CH_2OH)_2$, TsOH, C_6H_6; Ph_3P; iii, NaH, DMSO, Me_2CO; H_3O^+; iv, NaH, Me_2SO, MeCOEt

reaction conditions, by a straightforward Wittig reaction in dimethoxyethane at 80 °C using n-butyl-lithium as base and with a yield of 70% (determined by g.l.c.).

This method gave the two farnesenes by a six-stage synthesis and an overall yield of 34%. The failure to obtain a stereospecific reaction in the final stage required a preparative method of separation, which was solved economically by medium-pressure chromatography on silica loaded with 20% silver nitrate, eluting with ether–light petroleum.[22]

Pure farnesenes are very unstable in air and rapidly polymerize to a gummy solid; this made microanalysis difficult. The molar extinction coefficients given by Anet[4] of 11 300 for (*Z*,*E*)-α-farnesene must be revised. We obtained ε 23 150 for the (*Z*,*E*) isomer and ε 22 350 for the (*Z*,*Z*) isomer (Anet[4] gave ε 22 500). Values for the more important ^{1}H n.m.r. absorptions for the two isomers are compared with literature values[4,23] in the Table. The chief differences are in the methyl signals; in (*Z*,*E*)-α-farnesene they appear as four singlets, in (*Z*,*Z*)-α-farnesene two of the methyls coincide at δ 1.67. The downfield shift from δ 1.62 to 1.67 is related to the C-7 methyl. Such shifts have been reported by several authors for related compounds.[18,24–27] I.r. spectra were recorded but they showed only minor differences.[1] The mass spectral data for the pure isomers corresponded to those given by Anet[4] for the substances obtained by dehydrating nerolidol, and the (*Z*,*E*)-α-farnesene was clearly identical with the *Myrmica* ant farnesene. Mass spectra were recorded on several instruments; the small differences noted by Anet[4] are consistent and indeed can be used reliably for identifying farnesene isomers.

The 7-methyloct-6-en-3-one required for homofarnesene (**2**) and the 7-methylnon-6-en-3-one required for bishomofarnesene (**3**) and trishomofarnesene (**4**) were not commercially available. They were prepared from 4-chlorobutyryl chloride (**13**) as outlined in Scheme 2. Grignard addition in the presence of ferric chloride[28] gave the chloroketone (**14**), which was converted into the acetal (**16**) after halogen exchange, and thence to the triphenylphosphonium iodide (**17**) using conditions similar to those used by Findlay *et al.* to prepare 6-methyloct-5-en-2-one.[29] Wittig reaction between the phosphonium salt (**17**) and acetone gave the ketone (**18**) and between the salt and butanone gave the ketone (**19**). The yield of methyloctenone recorded by Findlay *et al.*[29] was 83% based on butanone, with an excess of phosphonium salt. The salt used here was prepared by a multistage synthesis and yields were 44% for (**18**) and 49% for (**19**) based on the phosphonium salt. The ketone (**19**) consisted of a mixture of (*Z*) and (*E*) isomers in the ratio 66:34 determined by ^{13}C n.m.r. spectroscopy. By analogy with the insect juvenile hormones and faranal, a pheromone from the ant *Monomorium pharaonis*,[30] bishomofarnesene (**3**), and trishomofarnesene (**4**) are expected to have a (*Z*)-10 double bond; at present, the configuration is unknown. For proof, both isomers may have to be synthesized, but the isomers were not separated at this stage.

Wittig reagents normally react very sluggishly with ketones, but by careful choice of reaction conditions three Wittig reactions were successfully performed with ketones in the present work. However, attempts to prepare homofarnesenes by condensation of the phosphonium salt (**10**) with the ethyl ketone (**18**) gave very poor yields. In order to find the cause, parallel Wittig reactions using either the methyl ketone (**11**) or ethyl ketone (**18**) were carried out simultaneously, and a large difference in reactivity was found, presumably because of increased steric hindrance. Forcing conditions including higher temperature and longer reaction time to improve yield, caused either destruction of the product or isomerization to other farnesenes or allofarnesenes. The best yield (10% by g.l.c.) was found using two moles of butyl-lithium in dimethoxyethane at room temperature followed by heating to 84 °C or by heating to 134 °C for 2 h in a Carius tube. The isomers were separated by g.l.c. It is known that the (*Z*,*Z*) isomer of farnesene is eluted before the (*Z*,*E*) isomer[4] and this was confirmed after our synthesis of the two isomers; the structure of (**2**), excluding geometry, had been established by micro-ozonolysis.[11] The g.l.c. retention times and the mass spectrum of the later eluting product of the synthesis both confirmed its identity with the

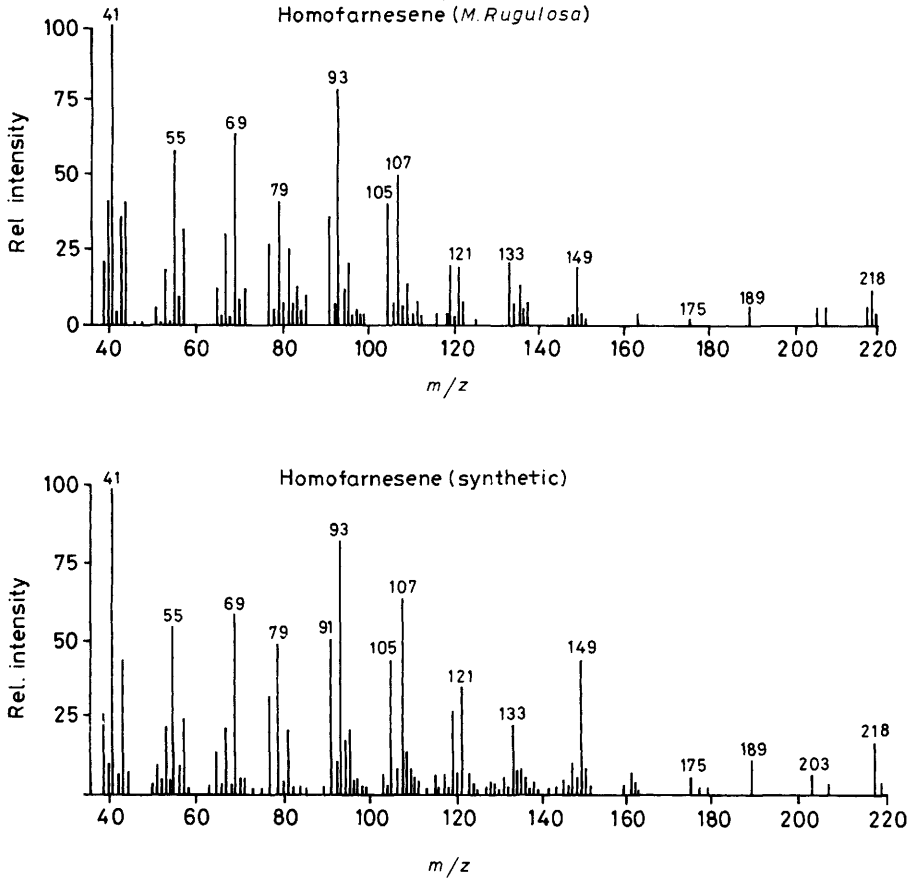


Figure 1. Mass spectra of synthetic (*Z,E*)-α-homofarnesene and homofarnesene from the Dufour gland of a *Myrmica* ant worker.

Table. ^{1}H N.m.r. spectral data for (*Z,E*)- and (*Z,Z*)-α-farnesenes

		CH_3				$^{\cdot}$-CH_2-CH_2-(4H)	=C-CH_2-C= (triplets)	-CH=(5H) (multiplet)	=CH-C= (quartets)
(*Z,E*)-α-	δ($CDCl_3$)	1.59	1.62	1.67	1.80	2.01(s)	2.79		6.66
							2.85	5.0—5.33	6.77
							2.93		6.84
									6.94
Lit.[23] (*Z,E*)-	δ(CCl_4)	1.60	1.65	1.69(3s,12H)		2.00	2.78	4.95—5.25	6.74
(*Z,Z*)-α-	δ($CDCl_3$)	1.60	1.67(6H)		1.80	2.00(d)	2.83	4.9—5.3	6.7
Lit.[4] (*Z,Z*)-α-	δ*	1.62	1.68	1.69	1.80		2.87		6.77

* Solvent not specified, either $CDCl_3$ or CCl_4.

Myrmica homofarnesene and established it as (*Z,E*)-α-homofarnesene (see Figure). The difficulties of separating and handling the small quantity of air-sensitive product prevented the recording of full spectral details. Unsuccessful attempts to complete the last stage of the synthesis in higher yield, such as using a sulphoxide[31] or sulphone[32] instead of the Wittig reagent are recorded elsewhere.[1]

Experimental

N.m.r. spectra were determined at 60 and 100 MHz for ^{1}H, at 25.14 MHz for ^{13}C and 40.48 MHz for ^{31}P.

Medium pressure liquid chromatography (m.p.l.c.) was performed using a MPL series II micropump (Metering Pumps, London) with a PTFE diaphragm pumphead (maximum pressure 100 p.s.i.). Samples were injected on-column through a Tefzel slider valve using a 10 ml Hamilton 1010 gas-tight syringe.

Purification of Solvents and Reagents.—Tetrahydrofuran (THF) was dried by distillation from sodium–benzophenone. Dimethyl sulphoxide was distilled under reduced pressure. Dimethoxyethane was dried over sodium and decanted. Diglyme was distilled from sodium. Solvents for m.p.l.c. were dried over 4A molecular sieves. Ethanol was dried by refluxing over and distillation from magnesium. Acetone for Wittig reactions was distilled from P_2O_5. Butan-2-one was distilled from anhydrous potassium carbonate. The titration method described by Winkle *et al.*[33] was used to check the concentration of n-butyl-lithium (Aldrich, Gillingham) in hexane solutions.

Use of Glove-bag.—A glove-bag which was flushed with nitrogen and sealed, with the necessary apparatus and materials inside, was used for the weighing, or measuring out of air- and moisture-sensitive reagents.

2-*Cyclopropylbut*-3-*yn*-2-*ol* (**6**).—Liquid ammonia (500 ml) was stirred mechanically in a 2-l 3-necked flask with cooling in a bath of liquid nitrogen–ethyl acetate. Ferric nitrate (0.2 g) and a few small pieces of sodium were added, and the remainder of the sodium (9.7 g, 0.42 g-atom) was added in portions. Stirring was continued for 30 min after the addition of the sodium was complete and before acetylene (from calcium carbide and water, dried by passage through conc. H_2SO_4) was bubbled in. The mixture became grey and then slowly blackened. The flow of acetylene was reduced and cyclopropyl methyl ketone (33.6 g, 0.4 mol), in an equal volume of diethyl ether, was added dropwise. The mixture was then allowed to warm up overnight when the ammonia evaporated. Diethyl ether was added and the mixture triturated with a solution of tartaric acid (16 g) in water (40 ml) with cooling in ice. The organic layer was decanted and the aqueous layer extracted with 3 portions of diethyl ether. The combined organic phases were washed with 5% aqueous tartaric acid and then water, dried (K_2CO_3), and evaporated. The residue was distilled under reduced pressure to give 2-cyclopropylbut-3-yn-2-ol (**6**) (33.9 g, 77%) b.p. 48—50 °C/15 mmHg, n_D^{21} 1.4572, (lit.,[17] gives b.p. 72—73 °C/40 mmHg, n_D^{21} 1.4565), δ (60 MHz; solvent $CDCl_3$; standard Me_4Si) 0.45 (4 H, d, *J* 7 Hz, cyclopropyl CH_2), 1.1 (1 H, m, J 7 Hz, cyclopropyl CH), 1.55 (3 H, s, CH_3), 2.3 (1 H, s, ≡CH), and 2.4 (1 H,br s, OH); $\nu_{max.}$ 3 400 (br, OH), 3 300 (≡C–H), and 2 100 cm^{-1} (weak C≡CH).

(Z)-6-*Bromo*-3-*methylhex*-3-*en*-1-*yne* (**7**).—2-Cyclopropylbut-3-yn-2-ol (39.8 g, 0.36 mol) was stirred for 15 min with 48% HBr (145 ml) with cooling in ice-water. The organic layer was separated and the aqueous layer extracted (×2) with light petroleum (b.p. 40—60 °C). The combined organic phases were washed with water, 5% aqueous $NaHCO_3$ and again with water, dried (K_2CO_3), and evaporated. The residue was distilled under reduced pressure, under nitrogen to give three fractions b.p. 62—64, 64—65, and 65—70 °C/12 mmHg which were identical (n.m.r.) The fractions were combined to give (*Z*)-6-bromo-3-methylhex-3-ene-1-yne (**7**) (55.8 g, 89%), δ_H (60 MHz; solvent $CDCl_3$; standard $SiMe_4$) 1.35 (3 H, d, *J* 1 Hz, CH_3), 2.8 (2 H, t, *J* 6 Hz, CH_2C=), 3.1 (1 H, s, C≡CH), 3.35 (2 H, t, *J* 6 Hz, CH_2Br), and 5.7 (1 H, t, *J* 6 Hz, CH=) (lit.,[17] gives b.p. 64 °C/10 mmHg).

(Z)-6-*Bromo*-3-*methylhexa*-1,3-*diene* (**8**).—A solution of 6-bromo-3-methylhex-3-en-1-yne (55.8 g, 0.32 mol) in methanol (200 ml) was stirred with palladium on barium sulphate (2 g) and quinoline (2 ml) under an atmosphere of hydrogen for 39 h until the required amount of hydrogen had been absorbed. The catalyst was filtered off and the methanol evaporated and replaced with light petroleum (b.p. 60—80 °C). The resulting solution was washed with dilute HCl and then water, dried (K_2CO_3), and evaporated. The residue was distilled under reduced pressure of nitrogen to give (*Z*)-6-*bromo*-3-*methylhexa*-1,3-*diene* (**8**) (46 g, 86%), b.p. 69—72 °C/13 mmHg [lit.[34] gives b.p. 72 °C/12 mmHg for a mixture of (*E*)- and (*Z*)-isomers]. (Found: C, 48.0; H, 6.3%; M^+ 174. $C_7H_{11}Br$ requires C, 48.0; H, 6.3%; *M*, 174); δ_H (100 MHz; solvent $CDCl_3$; standard $SiMe_4$) 1.8 (3 H, d, *J* 1 Hz, CH_3C=), 2.7 (2 H, t, 7 Hz, CH_2C=), 3.25 (2 H, t, 7 Hz, CH_2Br), 4.9—5.5 (3 H, m, CH_2= and CH=), 6.4—6.9 (1 H, dd, *J* 10 and 16 Hz, =CHC=); $\nu_{max.}$ 3 090, 3 010, 2960, 1 640, 1 600, 1 440br, 1 380, 1 270, 1 240, 1 205, 1 080, 985, and 910 cm^{-1}; $\lambda_{max.}$(EtOH) 233 nm (ε 18 200).

(Z)-6-*Iodo*-3-*methylhexa*-1,3-*diene* (**9**).—A solution of (*Z*)-6-bromo-3-methylhexa-1,3-diene (49.5 g, 0.28 mol) in acetone (600 ml) was treated with sodium iodide (85 g, 0.56 mol) at reflux for 8 h. After evaporation of the acetone, the residue was dissolved in water and extracted (×3) with ether. The combined extracts were washed with 0.05M-aqueous $Na_2S_2O_3$, dried ($MgSO_4$), and evaporated to give crude (Z)-6-*iodo*-3-*methylhexa*-1,3-*diene* (57.5 g, 92.5%), δ_H (100 MHz; solvent $CDCl_3$; standard $SiMe_4$) 1.8 (3 H, d, *J* 1 Hz, CH_3C=), 2.7 (2 H, t, *J* 7 Hz, CH_2C=), 3.0 (2 H, t, *J* 7 Hz, CH_2I), 4.9—5.4 (3 H, m, CH_2= and CH=) 6.3—6.8 (1 H, dd, *J* 16 and 10 Hz, =CHC=). This was converted into the phosphonium salt without further purification.

(Z)-4-*Methylhexa*-3,5-*dienyltriphenylphosphonium Iodide* (**10**).—A solution of 6-iodo-3-methylhexa-1,3-diene (23.8 g, 0.107 mol) and triphenylphosphine (29 g, 0.11 mol) in dimethylformamide (50 ml) was heated on a boiling water-bath for 4 h. The solution was then concentrated and on cooling crystallization occurred to give 12.3 g of salt (m.p. 131—136 °C) which was filtered off and washed with ether. Addition of ether to the filtrate produced further crystals (33.3 g, m.p. 130—135 °C) to give (Z)-4-*methylhexa*-3,5-*dienyltriphenylphosphonium iodide* (45.6 g, 88%) (Found: C, 62.05; H, 5.3. $C_{25}H_{26}IP$ requires C, 61.99; H, 5.41%); δ_H (100 MHz; solvent $CDCl_3$; standard $SiMe_4$) 1.6 (3 H, s, CH_3), 2.2—2.9 (2 H, br m, CH_2C=), 3.4—3.9 (2 H, br m, CH_2P), 4.9—5.5 (3 H, m, CH_2= and CH=) 6.0—6.5 (1 H dd, *J* 16 and 10 Hz, =CHC=), 7.6—7.8 (15 H, m, Ph) *m*/*z* 357 ($Ph_3PC_7H_{11}$).

(Z,E)- *and* (Z,Z)-α-*Farnesene* (**1**) *and* (**12**).—To a stirred suspension of 4-methylhexa-3,5-dienyltriphenylphosphonium iodide (**10**) (48.8 g, 0.1 mol) in dimethoxyethane (100 ml) under a N_2 atmosphere, a solution of n-butyl-lithium in hexane (1.6M; 1.25 ml, 0.2 mol) was added dropwise and stirred at room temperature for 30 min. The mixture was then cooled to 0 °C and 6-methylhept-5-en-2-one (**11**) (12.6 g, 0.1 mol) was added. The temperature was allowed to return slowly to ambient with stirring for 90 min. The mixture was then heated under reflux (84 °C) for 2.5 h. After cooling, the mixture was diluted with aqueous methanol and the products extracted with light petroleum (b.p. 40—60 °C). Gas chromatography of the residue on a 5% OV 101 column at 162 °C showed two peaks, R_t 3.2 and 3.5 min (yield 70% by g.l.c.). Distillation under reduced pressure gave a mixture (*Z*,*E*)- and (*Z*,*Z*)-α-farnesene in the ratio 1:2, b.p. 71—85 °C/0.15 mmHg.

Medium-pressure Chromatography of Farnesene Isomers.—A 1 g sample of the farnesene mixture was chromatographed on a 1 m × 15 mm column packed with 20% $AgNO_3$ on Kieselgel 60(230—400 mesh ASTM) eluting with 10% diethyl ether–light petroleum (b.p. 40—60 °C). 15-ml Fractions were collected with a fraction collector and analysed by gas chromatography on a 5 ft 3% OV 101 on Chromosorb W column (oven temperature 120 °C, N_2 flow rate 60 ml min^{-1}.

(Z,E)-α-*Farnesene* (**1**).—Fractions 62—93 from the medium-pressure column were combined and evaporated. The residue was purified by bulb-tube distillation at reduced pressure to give (*Z*,*E*)-α-farnesene, *m*/*z* 204 (M^+); δ_H (100 MHz; solvent $CDCl_3$; standard $SiMe_4$) 1.80, 1.67, 1.62, 1.59 (12 H, 4 s, CH_3), 2.01 (4 H, s, CH_2CH_2) 2.85 (2 H, t, *J* = Hz, =CCH_2C=), 5.0—5.33 (5 H, complex m, alkene), and 6.66—6.94 (1 H, q, *J* 10 and 16 Hz, =CHC=); $\nu_{max.}$ 3 100, 1 805, 1 640, 1 595, 1 150, 990, and 835 cm^{-1}; $\lambda_{max.}$(hexane) 233 nm (ε 23,150).

(Z,Z)-α-*Farnesene* (**12**).—Fractions 26—48 were combined and evaporated. Bulb-tube distillation under reduced pressure gave (*Z*,*Z*)-α-farnesene, *m*/*z* 204 (M^+); δ $CDCl_3$ 1.60, 1.67, 1.80 (12 H, 3 s, CH_3), 2.0 (4 H, d, CH_2CH_2), 2.83 (2 H, t, *J* Hz, =CCH_2C=), 4.9—5.3 (5 H, complex m, alkene), and 6.7 (1 H, q, *J* 10 and 16 Hz, =CHC=); $\nu_{max.}$ 3 090, 1 800, 1 640, 1 590, 1 135, 985, 900, and 830 cm^{-1}; $\lambda_{max.}$(hexane) 237 nm (ε 22,350).

6-*Chlorohexan*-3-*one* (**14**).—A solution of ethylmagnesium

bromide was prepared from ethyl bromide (84.5 g, 0.78 mol) and magnesium (18.8 g, 0.77 g-atom) in diethyl ether (300 ml) under nitrogen in a 3-necked round-bottomed flask. The solution was transferred under nitrogen by means of a ground-glass jointed, bent tube, inserted into one of the side necks of the flask, into a dropping funnel. A plug of glass wool in the tube was used to filter the solution which was then added dropwise, under nitrogen to a stirred solution of 4-chlorobutyryl chloride (**13**) (99 g, 0.70 mol) and anhydrous ferric chloride (3 g) in dry ether with cooling in a bath of liquid nitrogen–ethyl acetate. The mixture was stirred for 5 min after the addition was complete before being poured onto ice. The organic layer was separated and the aqueous layer extracted (× 2) with diethyl ether. The combined organic phases were washed with 10% aqueous Na_2CO_3 (× 2) and then water (× 2), dried ($MgSO_4$), and evaporated. Distillation of the residue under reduced pressure gave 6-chlorohexan-3-one (**14**) (64.6 g, 68%), b.p. 70—76 °C/12 mmHg (lit.[29] b.p. 67—70 °C/12 mmHg) δ (100 MHz; solvent $CDCl_3$; standard $SiMe_4$) 1.05 (3 H, t, *J* 7 Hz, CH_3), 2.05 (2 H, m, *J* 7 Hz, CH_2CCl), 2.50 (2 H, t, *J* 7 Hz, CH_2CEt) 2.55 (2 H, q, *J* 7 Hz, CH_2 of ethyl), 3.5 (2 H, t, *J* 7 Hz, CH_2Cl).

6-*Iodohexan*-3-*one* (**15**).—A solution of 6-chlorohexan-3-one (68 g, 0.51 mol) in acetone (1 l) was heated with sodium iodide (225 g, 1.5 mol) at reflux for 12 h. The acetone was evaporated and the residue dissolved in water and extracted (× 3) with diethyl ether. The combined extracts were washed with 0.05M-aqueous $Na_2S_2O_3$ and then water, dried ($MgSO_4$), and evaporated to give 110 g (96%) of 6-iodohexan-3-one (**15**) δ_H (100 MHz; solvent $CDCl_3$; standard $SiMe_4$) 1.0 (3 H, t, *J* 6Hz, CH_3), 1.9—2.3 (2 H, complex pattern, CH_2CI), 2.4—2.7 (4 H, complex pattern, × 2 $CH_2C{=}O$), 3.2 (2 H, t, *J* 6 Hz, CH_2I). This was converted into the acetal without further purification.

2-*Ethyl*-2-(3-*iodopropyl*)-1.3-*dioxolane* (**16**).—6-Iodohexan-3-one (110 g, 0.49 mol) was treated with freshly distilled ethylene glycol (82 ml, 1.5 mol) and toluene-*p* sulphonic acid (*ca.* 200 mg) in refluxing benzene (1.2 l) in a Dean-Stark apparatus until no more water was collected (13 h). The mixture was allowed to cool before it was neutralized with anhydrous K_2CO_3, washed with 5% aqueous $NaHCO_3$, (× 3) water, 0.05M-aqueous $Na_2S_2O_3$, and finally with water, dried ($MgSO_4$), and evaporated. The residue was distilled under reduced pressure to give, after a small forerun, two fractions b.p. 78—89 °C and 89—92 °C/0.25 mmHg which were identical (n.m.r.). The fractions were combined to give 2-*ethyl*-2-(3-*iodopropyl*)-1,3-*dioxolane* (**16**) (97.6 g, 74%) (Found: C, 35.65; H, 5.83%; M^+, 270. $C_8H_{15}IO_2$ requires C, 35.57; H, 5.61%; *M*, 270); δ_H (60 MHz; solvent $CDCl_3$; standard $SiMe_4$) 0.9 (3 H, t, *J* 7 Hz, CH_3), 1.4—2.0 (6 H, complex pattern, 2 × CH_2CO and CH_2Cl), 3.15 (2 H, t, *J* 7 Hz, CH_2I), and 3.85 (4 H, s, 2 × CH_2O).

3-(2-*Ethyl*-1,3-*dioxolan*-2-*yl*)*propyltriphenylphosphonium Iodide* (**17**).—A solution of 2-ethyl-2-(3-iodopropyl)-1,3-dioxolane (53.8 g, 0.20 mol) and triphenylphosphine (52.2 g, 0.20 mol) in dimethylformamide (50 ml) was boiled under reflux for 6 h. On cooling, crystallization occurred to give 76.1 g of the phosphonium salt (m.p. 199—202 °C) which was filtered off, washed with diethyl ether, and dried *in vacuo*. Further crystals (12 g; m.p. 168—188 °C) were obtained by adding diethyl ether to the filtrate to give a total of 88.1 g (83%) of 3-(2-*ethyl*-1,3-*dioxolan*-2-*yl*)*propyltriphenylphosphonium iodide* (**17**) (Found: C, 58.75; H, 5.7%; M^+, 405 for phosphonium ion. $C_{26}H_{30}IO_2P$ requires C, 58.65; H, 5.69%; *M*, 405 for phosphonium ion); δ_H (60 MHz; solvent $CDCl_3$; standard $SiMe_4$) 0.8 (3 H, t, *J* 7 Hz, CH_3), 1.5 (2 H, q, *J* 7 Hz, ethyl CH_2), 1.2—2.2 (4 H, br m, 2 × CH_2), 3.3—3.9 (2 H, br m, CH_2P), 3.8 (4 H, s, 2 × OCH_2) and 7.6—7.8 (15 H, m, Ph); $\nu_{max.}$(Nujol) 1 580, 1 430, 1 110, 1 060, 1 030, 995, and 905 cm^{-1}.

7-*Methyloct*-6-*en*-3-*one* (**18**).—In a dry 1-l, 3-necked flask fitted with reflux condenser, dropping funnel, and N_2 inlet and outlet, sodium hydride (50% dispersion; 10g, 0.208 mol) was washed with light petroleum (b.p. 30—40 °C) and then covered with dimethyl sulphoxide (200 ml; dried by distillation under reduced pressure and stored over molecular sieves). The suspension was stirred magnetically for 30 min at 80 °C and then cooled to 30 °C before addition of 3-(2-ethyl-1,3-dioxolan-2-yl)propyltriphenylphosphonium iodide (100 g, 0.19 mol) in dimethyl sulphoxide (300 ml). Stirring was continued for 1.5 h at 30 °C before addition of acetone (14 ml, 0.193 mol) in DMSO (40 ml). The mixture was stirred overnight under nitrogen before addition of water and extraction with light petroleum (b.p. 30—40 °C) (× 2). The combined extracts were washed with water (× 2), dried ($MgSO_4$), and evaporated to give 2-*ethyl*-2-(4-*methylpent*-3-*enyl*)-1,3-*dioxolane* (18.7 g). The crude acetal was dissolved in tetrahydrofuran (180 ml) and stirred overnight with 3% aqueous HCl (180 ml). The organic layer was separated and the aqueous layer extracted with light petroleum (b.p. 40—60 °C). The combined organic phases were washed (× 2) with water, dried ($MgSO_4$), and evaporated. The residue was distilled under reduced pressure to give 7-*methyloct*-6-*en*-3-*one* (**18**) (11.8 g, 44%), b.p. 77—84 °C/15 mmHg (Found: C, 76.74; H, 11.53%. $C_9H_{16}O$ requires C, 77.09; H, 11.50%); δ_H (60 MHz; solvent $CDCl_3$; standard $SiMe_4$) 1.0 (3 H, t, *J* 7 Hz, ethyl CH_3), 1.65 [6 H, d, *J* 4 Hz, $=C(CH_3)_2$], 2.2—2.6 (6 H, complex pattern, 3 × CH_2), 5.0 (1 H, br m, CH=); $\nu_{max.}$ 2 970, 2 930, 1 710, 1 670, 1 445, 1 410, 1 380, 1 115, and 1 020 cm^{-1}.

7-*Methylnon*-6-*en*-3-*one* (**19**).—This compound was prepared using the method described for 7-methyloct-6-en-3-one using sodium hydride (50% dispersion; 6 g, 0.125 mol) in dimethyl sulphoxide (100 ml) and the phosphonium salt (66 g, 0.116 mol) in DMSO (150 ml). Butan-2-one (10.4 ml; 0.116 mol) in DMSO (20 ml) was added after the mixture had been stirred for 70 min at 30 °C. After the mixture had been stirred for a further 2 h an excess of butan-2-one was added and stirring was continued overnight at room temperature. Water was added and the mixture extracted (× 3) with light petroleum (b.p. 30—40 °C). The combined extracts were washed (× 2) with water, dried ($MgSO_4$), and evaporated. The aqueous phase was filtered to remove the insoluble solid and extracted again (× 2) with light petroleum. The combined extracts were washed, dried, and evaporated as above to give a further 2 g of crude product. The total crude acetal (14.9 g) was dissolved in tetrahydrofuran (140 ml) and treated with an equal volume of 3% aqueous HCl. Work-up as described above and distillation of the residue under reduced pressure gave 7-*methylnon*-6-*en*-3-*one* (**19**) (8.8 g, 49%), b.p. 92—96 °C/15 mmHg; δ_H (60 MHz; solvent $CDCl_3$; standard $SiMe_4$) 0.9 (3 H, t, *J* 7 Hz, ethyl CH_3), 1.0 (3 H, t, *J* 7 Hz, ethyl CH_3), 1.6 (3 H, d, *J* 2 Hz, $CH_3C{=}$), 2.0 (2 H, q, *J* 7 Hz, ethyl CH_2), 2.3 (4 H, m, CH_2CH_2), 2.35 (2 H, q, *J* 7 Hz, ethyl CH_2), and 4.95 (1 H, br m, CH=). The ^{13}C n.m.r. spectrum of the product showed that it was a mixture of 66% *E* and 34% *Z* isomer.

Homofarnesene (**2**).—In a dry nitrogen-flushed Carius tube, (*Z*)-4-methylhexa-3,5-dienyltriphenylphosphonium iodide (0.96 g, 1.98 mmol) was suspended in dimethoxyethane. The tube was fitted with a rubber septum and n-butyl-lithium in hexane (1.6M; 3 ml, 4.8 mmol) and 7-methyloct-6-en-3-one (0.3 ml, 1.98 mmol) were introduced into the tube *via* a syringe. The tube was sealed, placed inside the outer metal tube, and heated in a muffle furnace at 135 °C for 2 h. The cooled tube was opened and the contents dissolved in aqueous methanol and extracted (× 2)

with light petroleum (b.p. 40—60 °C). The combined extracts were washed with aqueous methanol (×2) and then water, dried ($MgSO_4$), and evaporated. The crude product was examined by gas chromatography which showed that there were two components of R_t 4.1 and 4.4 min on 3% OV-101 at 161 °C and 3.4 and 3.8 min on 5% DEGS at 129 °C, using a nitrogen flow of 60 ml min^{-1} with both columns. Ant homofarnesene had R_t values of 4.4 and 3.8 min on these columns respectively, under the same conditions. Their mass spectra were similar and clearly those of homofarnesene (M^+, 218, m/z 203, 189, 175, and 149). The mass spectrum obtained by g.c.–mass spectroscopy of the component with longer retention time was identical to that of ant homofarnesene (see Figure).

Acknowledgements

We thank Dr. J. A. Pickett for farnesene mass spectra and Professor I. T. Millar for a critical reading of our manuscript.

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Received 18*th June* 1984; *Paper* 4/1025